

For Public Disclosure

Mlett 304472

Certified Mail No.:

TSCA Document Control Office (7407M)
ATTN: TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001



8 E H Q - 0 7 - 1 6 7 4 9

Company Sanitized

07 May 09 AM 10:53

RECEIVED
OPI
MAY 10 2009

Re: TSCA 8(e) Supplemental Notice for 8EHQ-07-16749: Draft Sub-chronic Toxicity
Reproductive/Developmental Data on 1,2-Diaminocyclohexane

Dear Sir:

is submitting this letter to supplement its previous submissions concerning draft results from an OECD 422, sub-chronic toxicity study on 1,2-Diaminocyclohexane, CASRN 694-83-7, with draft reproductive/developmental data.

As discussed in our previous February 28, 2007 submission, gross pathology results from a 28-day toxicity study with 1,2-Diaminocyclohexane, in drinking water, revealed a pale discoloration (see Attachments 1) of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in 5 of 10 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg.

also recently submitted additional preliminary results on April 2, 2007 (see Attachment 2) from this study. Certain clinical biochemistry findings in this preliminary report supplemented our earlier findings regarding the liver discoloration described above. High serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities, as well as elevated alkaline (ALP) phosphatase (exact levels not reported) and cholesterol levels were noted in the high dose male rats. High serum ALT and AST activities were also reported in high dose females, although no gross liver effects were noted.

Further preliminary results (Attachment 3, with appendices), and the basis for this supplemental submission, indicate that the average and total number of living pups per litter was reduced in the 500 mg/kg high dose group (6.9 pups/litter) when compared to concurrent controls (16.0 pups/litter). Also, increased postnatal loss was noted at 150 and 500 mg/kg, resulting in a reduced viability index.

These findings do not necessarily indicate that 1,2-Diaminocyclohexane is a specific reproductive or developmental toxicant. Although maternal toxicity is apparent at the high dose, and likely at the mid- dose,



8 9 0 7 0 0 0 0 2 6 6 7 S

For Public Disclosure

EPA guidelines generally require reporting of Reproductive/Developmental effects at any dose regardless of the presence of maternal toxicity.

The above information is from a draft study that has not yet been completed. [REDACTED] will submit the final version of the study to EPA when it becomes available.

This report is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at [REDACTED]

Sincerely,

Attachments

For Public Disclosure

ATTACHMENT 1

8EHQ-07-16749

8(e) Notification Letter for 1,2-Diaminocyclohexane

Public Version

TRACKING Numbr []

[]
TSCA Document Control Office (7407M)
ATTN: TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001

Re: TSCA 8(e) Submission for draft Sub-chronic Toxicity data on 1,2-Diaminocyclohexane

Dear Sir:

[] is submitting draft results from an OECD 422, sub-chronic toxicity study on 1,2-Diaminocyclohexane [] CASRN 694-83-7, []

Gross pathology results from a 28-day toxicity study with [] in drinking water, revealed a pale discoloration of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in 5 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg.

In order to further evaluate whether the pale discoloration and/or organ weight changes are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment related effect on the liver in the high dose male rats.

The above information is from a draft study that has not yet been completed. [] will submit the final version of the study to EPA when it becomes available.

This report is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at []

Sincerely,

[]
Attachments []

MACROSCOPIC FINDINGS
MALES
ALL NECROPSIES

ANIMAL ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)		
1	No findings noted	Scheduled necropsy, 08Feb2007
2	No findings noted	Scheduled necropsy, 08Feb2007
3	No findings noted	Scheduled necropsy, 08Feb2007
4	No findings noted	Scheduled necropsy, 08Feb2007
5	Kidneys	Right side: pelvic dilation.
6	Bone	Tail apex: bent.
7		No findings noted
8		No findings noted
9		No findings noted
10		No findings noted
GROUP 2 (50 MG/KG)		
11	No findings noted	Scheduled necropsy, 08Feb2007
12	No findings noted	Scheduled necropsy, 08Feb2007
13	No findings noted	Scheduled necropsy, 08Feb2007
14	No findings noted	Scheduled necropsy, 08Feb2007
15	Bone	Tail apex: bent.
16		No findings noted
17		No findings noted
18		No findings noted
19		No findings noted
20	Seminal vesicles	Right side: reduced in size.
GROUP 3 (150 MG/KG)		
21	No findings noted	Scheduled necropsy, 08Feb2007
22	No findings noted	Scheduled necropsy, 08Feb2007
23	No findings noted	Scheduled necropsy, 08Feb2007
24	No findings noted	Scheduled necropsy, 08Feb2007
25	No findings noted	Scheduled necropsy, 08Feb2007
26	No findings noted	Scheduled necropsy, 08Feb2007
27	No findings noted	Scheduled necropsy, 08Feb2007
28	No findings noted	Scheduled necropsy, 08Feb2007
29	No findings noted	Scheduled necropsy, 08Feb2007
30	Seminal vesicles	Left side: reduced in size.
GROUP 4 (500 MG/KG)		
31	Liver	Discolouration, pale.
32		No findings noted
33	Liver	Discolouration, pale.
34		No findings noted
35	Liver	Discolouration, pale.
36	Liver	Discolouration, pale.
37		No findings noted
38		No findings noted
39		No findings noted
40	Liver	Discolouration, pale.

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
1	451	2.03	1.348	12.08	0.619
2	413	2.02	1.319	10.65	0.324
3	444	---	---	---	---
4	410	1.89	1.149	9.95	0.417
5	421	---	---	---	---
6	437	2.13	1.240	11.73	0.532
7	451	2.14	1.259	12.94	0.445
8	397	---	---	---	---
9	380	---	---	---	---
10	437	---	---	---	---
GROUP 2 (50 MG/KG)					
11	453	---	---	---	---
12	407	2.21	1.273	10.47	0.334
13	410	2.03	1.285	10.75	0.338
14	420	2.13	1.257	10.65	0.369
15	381	---	---	---	---
16	395	2.20	1.405	10.41	0.450
17	410	2.11	1.391	9.82	0.269
18	408	---	---	---	---
19	422	---	---	---	---
20	458	---	---	---	---
GROUP 3 (150 MG/KG)					
21	411	2.25	1.389	11.26	0.405
22	459	2.11	1.490	11.30	0.556
23	375	1.95	1.212	9.74	0.236
24	386	2.11	1.203	9.23	0.311
25	464	2.01	1.447	13.12	0.386
26	400	---	---	---	---
27	455	---	---	---	---
28	425	---	---	---	---
29	396	---	---	---	---
30	388	---	---	---	---
GROUP 4 (500 MG/KG)					
31	412	2.15	1.405	12.49	0.242
32	410	2.11	1.380	11.50	0.347
33	410	---	---	---	---
34	408	2.07	1.453	12.90	0.284
35	381	2.06	1.446	12.98	0.305
36	384	2.08	1.398	12.44	0.248
37	391	---	---	---	---
38	411	---	---	---	---
39	393	---	---	---	---
40	428	---	---	---	---

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)					
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1.448
3	---	---	---	4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5	---	---	---	4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.085	1.250	4.01	1.229
8	---	---	---	4.10	1.142
9	---	---	---	3.86	1.344
10	---	---	---	4.25	1.353
GROUP 2 (50 MG/KG)					
11	---	---	---	3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15	---	---	---	3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18	---	---	---	3.72	1.284
19	---	---	---	3.92	1.313
20	---	---	---	3.78	1.199
GROUP 3 (150 MG/KG)					
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26	---	---	---	3.86	1.074
27	---	---	---	3.69	1.157
28	---	---	---	3.79	1.176
29	---	---	---	4.21	1.166
30	---	---	---	3.70	1.158
GROUP 4 (500 MG/KG)					
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33	---	---	---	3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37	---	---	---	3.87	0.886
38	---	---	---	4.57	1.148
39	---	---	---	3.84	1.172
40	---	---	---	4.35	1.124

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
1	451	0.45	0.299	2.68	0.137
2	413	0.49	0.319	2.58	0.078
3	444	---	---	---	---
4	410	0.46	0.280	2.43	0.102
5	421	---	---	---	---
6	437	0.49	0.284	2.68	0.122
7	451	0.47	0.279	2.87	0.099
8	397	---	---	---	---
9	380	---	---	---	---
10	437	---	---	---	---
GROUP 2 (50 MG/KG)					
11	453	---	---	---	---
12	407	0.54	0.313	2.57	0.082
13	410	0.49	0.313	2.62	0.082
14	420	0.51	0.299	2.53	0.088
15	381	---	---	---	---
16	395	0.56	0.356	2.63	0.114
17	410	0.51	0.339	2.39	0.066
18	408	---	---	---	---
19	422	---	---	---	---
20	458	---	---	---	---
GROUP 3 (150 MG/KG)					
21	411	0.55	0.338	2.74	0.099
22	459	0.46	0.325	2.46	0.121
23	375	0.52	0.323	2.60	0.063
24	386	0.55	0.312	2.39	0.081
25	464	0.43	0.312	2.83	0.083
26	400	---	---	---	---
27	455	---	---	---	---
28	425	---	---	---	---
29	396	---	---	---	---
30	388	---	---	---	---
GROUP 4 (500 MG/KG)					
31	412	0.52	0.341	3.03	0.059
32	410	0.51	0.337	2.80	0.085
33	410	---	---	---	---
34	408	0.51	0.356	3.16	0.070
35	381	0.54	0.380	3.41	0.080
36	384	0.54	0.364	3.24	0.065
37	391	---	---	---	---
38	411	---	---	---	---
39	393	---	---	---	---
40	428	---	---	---	---

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)					
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.265	1.09	0.351
3	---	---	---	0.92	0.306
4	0.69	0.017	0.190	0.93	0.285
5	---	---	---	1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8	---	---	---	1.03	0.288
9	---	---	---	1.02	0.354
10	---	---	---	0.97	0.310
GROUP 2 (50 MG/KG)					
11	---	---	---	0.81	0.298
12	0.79	0.016	0.230	1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15	---	---	---	0.95	0.317
16	0.76	0.015	0.275	0.91	0.327
17	0.86	0.016	0.199	0.73	0.250
18	---	---	---	0.91	0.315
19	---	---	---	0.93	0.311
20	---	---	---	0.83	0.262
GROUP 3 (150 MG/KG)					
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.69	0.016	0.264	0.93	0.268
26	---	---	---	0.97	0.269
27	---	---	---	0.81	0.254
28	---	---	---	0.89	0.277
29	---	---	---	1.06	0.294
30	---	---	---	0.95	0.298
GROUP 4 (500 MG/KG)					
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.020	0.247	0.97	0.222
33	---	---	---	0.97	0.258
34	0.85	0.021	0.224	1.04	0.253
35	0.81	0.020	0.219	0.94	0.268
36	0.75	0.016	0.214	1.00	0.259
37	---	---	---	0.99	0.227
38	---	---	---	1.11	0.279
39	---	---	---	0.98	0.298
40	---	---	---	1.02	0.263

For Public Disclosure

ATTACHMENT 2

TSCA 8(e) Supplemental Information to 8EHQ-07-16749: Draft Corroborative Sub-chronic Toxicity Clinical
Biochemistry Data on 1,2-Diaminocyclohexane

Public Version

TRACKING Number: []

TSCA Document Control Office (7407M)
ATTN: TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001

Re: TSCA 8(e) Supplemental Information to : Draft Corroborative Sub-chronic Toxicity
Clinical Biochemistry Data on 1,2-Diaminocyclohexane

Dear Sir:

[] is submitting this letter to supplement with corroborative draft clinical biochemical data its previous submission concerning draft results from an OECD 422, sub-chronic toxicity study on 1,2-Diaminocyclohexane [] CASRN 694-83-7, conducted by []

As discussed in our [] submission (see attachment 1), gross pathology results from a 28-day toxicity study with [] in drinking water, revealed a pale discoloration of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in 5 of 10 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg.

[] has recently reviewed additional preliminary results (see Attachment 2) from this study. Certain clinical biochemistry findings in this preliminary report supplement our earlier findings regarding the liver discoloration described above. High serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities, as well as elevated alkaline (ALP) phosphatase (exact levels not reported) and cholesterol levels, were noted in the high dose male rats. High serum ALT and AST activities were also reported in high dose females, although no gross liver effects were noted.

Elevated ALT, AST, ALP, and cholesterol may be indicative of possible liver damage. Although biochemical changes are not routinely reportable under TSCA 8(e) for sub-chronic studies, these changes may be considered corroborative or supplementary data to the information already shared with the Agency concerning the effects of [] on male rat liver discoloration.

Public Version

In order to further evaluate whether the pale discoloration and/or organ weight changes, or clinical biochemistry findings, are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment-related effect on the liver in the high dose male rats.

The above information is from a draft study that has not yet been completed. Because this submitted data, as well as the previously submitted data (Attachment 1), are from a draft study, please note that there are two Laboratory Project numbers associated with these submissions, [] (Attachment 1) and [] (Attachment 2). Both Project numbers are from the same OECD 422 study and are numbered, in draft form, to reflect internal laboratory coding conventions. [] will submit the final version of the study to EPA when it becomes available.

These reports are being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at []

Sincerely,

[]
[]

Attachments

[] []

Public Version

ATTACHMENT 1

8(e) Notification Letter for 1,2-Diaminocyclohexane
[]

[]

Public Version

TRACKING Numbr. []

[]
TSCA Document Control Office (7407M)
ATTN: TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001

Re: TSCA 8(e) Submission for draft Sub-chronic Toxicity data on 1,2-Diaminocyclohexane

Dear Sir:

[] is submitting draft results from an OECD 422, sub-chronic toxicity study on 1,2-Diaminocyclohexane [] CASRN 694-83-7, []

Gross pathology results from a 28-day toxicity study with [] in drinking water, revealed a pale discoloration of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in 5 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg.

In order to further evaluate whether the pale discoloration and/or organ weight changes are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment related effect on the liver in the high dose male rats.

The above information is from a draft study that has not yet been completed. [] will submit the final version of the study to EPA when it becomes available.

This report is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at []

Sincerely,

[]
Attachments []

MACROSCOPIC FINDINGS
MALES
ALL NECROPSIES

ANIMAL ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)		
1	No findings noted	Scheduled necropsy, 08Feb2007
2	No findings noted	Scheduled necropsy, 08Feb2007
3	No findings noted	Scheduled necropsy, 08Feb2007
4	No findings noted	Scheduled necropsy, 08Feb2007
5 Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 08Feb2007
6 Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
7	No findings noted	Scheduled necropsy, 08Feb2007
8	No findings noted	Scheduled necropsy, 08Feb2007
9	No findings noted	Scheduled necropsy, 08Feb2007
10	No findings noted	Scheduled necropsy, 08Feb2007
GROUP 2 (50 MG/KG)		
11	No findings noted	Scheduled necropsy, 08Feb2007
12	No findings noted	Scheduled necropsy, 08Feb2007
13	No findings noted	Scheduled necropsy, 08Feb2007
14	No findings noted	Scheduled necropsy, 08Feb2007
15 Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
16	No findings noted	Scheduled necropsy, 08Feb2007
17	No findings noted	Scheduled necropsy, 08Feb2007
18	No findings noted	Scheduled necropsy, 08Feb2007
19	No findings noted	Scheduled necropsy, 08Feb2007
20 Seminal vesicles	Right side: reduced in size.	Scheduled necropsy, 08Feb2007
GROUP 3 (150 MG/KG)		
21	No findings noted	Scheduled necropsy, 08Feb2007
22	No findings noted	Scheduled necropsy, 08Feb2007
23	No findings noted	Scheduled necropsy, 08Feb2007
24	No findings noted	Scheduled necropsy, 08Feb2007
25	No findings noted	Scheduled necropsy, 08Feb2007
26	No findings noted	Scheduled necropsy, 08Feb2007
27	No findings noted	Scheduled necropsy, 08Feb2007
28	No findings noted	Scheduled necropsy, 08Feb2007
29	No findings noted	Scheduled necropsy, 08Feb2007
30 Seminal vesicles	Left side: reduced in size.	Scheduled necropsy, 08Feb2007
GROUP 4 (500 MG/KG)		
31 Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
32	No findings noted	Scheduled necropsy, 08Feb2007
33 Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
34	No findings noted	Scheduled necropsy, 08Feb2007
35 Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
36 Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
37	No findings noted	Scheduled necropsy, 08Feb2007
38	No findings noted	Scheduled necropsy, 08Feb2007
39	No findings noted	Scheduled necropsy, 08Feb2007
40 Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
1	451	2.03	1.348	12.08	0.619
2	413	2.02	1.319	10.65	0.324
3	444	---	---	---	---
4	410	1.89	1.149	9.95	0.417
5	421	---	---	---	---
6	437	2.13	1.240	11.73	0.532
7	451	2.14	1.259	12.94	0.445
8	397	---	---	---	---
9	380	---	---	---	---
10	437	---	---	---	---
GROUP 2 (50 MG/KG)					
11	453	---	---	---	---
12	407	2.21	1.273	10.47	0.334
13	410	2.03	1.285	10.75	0.338
14	420	2.13	1.257	10.65	0.369
15	381	---	---	---	---
16	395	2.20	1.405	10.41	0.450
17	410	2.11	1.391	9.82	0.269
18	408	---	---	---	---
19	422	---	---	---	---
20	458	---	---	---	---
GROUP 3 (150 MG/KG)					
21	411	2.25	1.389	11.26	0.405
22	459	2.11	1.490	11.30	0.556
23	375	1.95	1.212	9.74	0.236
24	386	2.11	1.203	9.23	0.311
25	464	2.01	1.447	13.12	0.386
26	400	---	---	---	---
27	455	---	---	---	---
28	425	---	---	---	---
29	396	---	---	---	---
30	388	---	---	---	---
GROUP 4 (500 MG/KG)					
31	412	2.15	1.405	12.49	0.242
32	410	2.11	1.380	11.50	0.347
33	410	---	---	---	---
34	408	2.07	1.453	12.90	0.284
35	381	2.06	1.446	12.98	0.305
36	384	2.08	1.398	12.44	0.248
37	391	---	---	---	---
38	411	---	---	---	---
39	393	---	---	---	---
40	428	---	---	---	---

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)					
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1.448
3	---	---	---	4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5	---	---	---	4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.085	1.250	4.01	1.229
8	---	---	---	4.10	1.142
9	---	---	---	3.86	1.344
10	---	---	---	4.25	1.353
GROUP 2 (50 MG/KG)					
11	---	---	---	3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15	---	---	---	3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18	---	---	---	3.72	1.284
19	---	---	---	3.92	1.313
20	---	---	---	3.78	1.199
GROUP 3 (150 MG/KG)					
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26	---	---	---	3.86	1.074
27	---	---	---	3.69	1.157
28	---	---	---	3.79	1.176
29	---	---	---	4.21	1.166
30	---	---	---	3.70	1.158
GROUP 4 (500 MG/KG)					
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33	---	---	---	3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37	---	---	---	3.87	0.886
38	---	---	---	4.57	1.148
39	---	---	---	3.84	1.172
40	---	---	---	4.35	1.124

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
1	451	0.45	0.299	2.68	0.137
2	413	0.49	0.319	2.58	0.078
3	444	---	---	---	---
4	410	0.46	0.280	2.43	0.102
5	421	---	---	---	---
6	437	0.49	0.284	2.68	0.122
7	451	0.47	0.279	2.87	0.099
8	397	---	---	---	---
9	380	---	---	---	---
10	437	---	---	---	---
GROUP 2 (50 MG/KG)					
11	453	---	---	---	---
12	407	0.54	0.313	2.57	0.082
13	410	0.49	0.313	2.62	0.082
14	420	0.51	0.299	2.53	0.088
15	381	---	---	---	---
16	395	0.56	0.356	2.63	0.114
17	410	0.51	0.339	2.39	0.066
18	408	---	---	---	---
19	422	---	---	---	---
20	458	---	---	---	---
GROUP 3 (150 MG/KG)					
21	411	0.55	0.338	2.74	0.099
22	459	0.46	0.325	2.46	0.121
23	375	0.52	0.323	2.60	0.063
24	386	0.55	0.312	2.39	0.081
25	464	0.43	0.312	2.83	0.083
26	400	---	---	---	---
27	455	---	---	---	---
28	425	---	---	---	---
29	396	---	---	---	---
30	388	---	---	---	---
GROUP 4 (500 MG/KG)					
31	412	0.52	0.341	3.03	0.059
32	410	0.51	0.337	2.80	0.085
33	410	---	---	---	---
34	408	0.51	0.356	3.16	0.070
35	381	0.54	0.380	3.41	0.080
36	384	0.54	0.364	3.24	0.065
37	391	---	---	---	---
38	411	---	---	---	---
39	393	---	---	---	---
40	428	---	---	---	---

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)					
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.265	1.09	0.351
3	---	---	---	0.92	0.306
4	0.69	0.017	0.190	0.93	0.285
5	---	---	---	1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8	---	---	---	1.03	0.288
9	---	---	---	1.02	0.354
10	---	---	---	0.97	0.310
GROUP 2 (50 MG/KG)					
11	---	---	---	0.81	0.298
12	0.79	0.016	0.230	1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15	---	---	---	0.95	0.317
16	0.76	0.015	0.275	0.91	0.327
17	0.86	0.016	0.199	0.73	0.250
18	---	---	---	0.91	0.315
19	---	---	---	0.93	0.311
20	---	---	---	0.83	0.262
GROUP 3 (150 MG/KG)					
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.69	0.016	0.264	0.93	0.268
26	---	---	---	0.97	0.269
27	---	---	---	0.81	0.254
28	---	---	---	0.89	0.277
29	---	---	---	1.06	0.294
30	---	---	---	0.95	0.298
GROUP 4 (500 MG/KG)					
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.020	0.247	0.97	0.222
33	---	---	---	0.97	0.258
34	0.85	0.021	0.224	1.04	0.253
35	0.81	0.020	0.219	0.94	0.268
36	0.75	0.016	0.214	1.00	0.259
37	---	---	---	0.99	0.227
38	---	---	---	1.11	0.279
39	---	---	---	0.98	0.298
40	---	---	---	1.02	0.263

[]

Public Version

ATTACHMENT 2

Clinical Biochemical Data for 1,2-Diaminocyclohexane (

From OECD 422, sub-chronic toxicity study

[]

ATTACHMENT 2

INTRODUCTION

Dose Level

- Group 1: 0 mg/kg body weight (Milli-U water)
Group 2: 50 mg/kg body weight
Group 3: 150 mg/kg body weight
Group 4: 500 mg/kg body weight

The purpose of this study was to evaluate the potential toxic effects of the test substance when administered to rats for a minimum of 28 days and to evaluate the potential of the test substance to affect male and female reproductive performance such as gonadal function, mating behaviour, conception, parturition and early postnatal development.

MATERIALS AND METHODS

Allocation

Group	Dose level mg/kg b.w./day	Number of animals		Animals numbers	
		F ₀ males	F ₀ females	males	females
1	0	10	10	01-10	41-50
2	50	10	10	11-20	51-60
3	150	10	10	21-30	61-70
4	500	10	10	31-40	71-80

RESULTS

Mortality

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of the pups. One female at 500 mg/kg (Female 79) was sacrificed due to litter loss on Day 2 of lactation. This animal had five pups, three pups were found dead on Day 1 of lactation, two other pups were found dead on Day 2 of lactation.

Clinical signs

Slight to moderate salivation was noted in all males and females treated at 500 mg/kg. Furthermore, incidentally rales was noted in two males at 500 mg/kg (Males 37 and 38) and piloerection was noted in one female at 500 mg/kg (Female 79) at the end of treatment.

Yellow discolouration of the urine was noted in all animals of Groups 2, 3 and 4 in a dose dependant manner.

Other clinical signs (scabs, chromodacryorrhoea, broken tail apex, diarrhoea and alopecia) were considered unrelated to treatment.

Body weight

Reduced body weight gain was noted in males treated at 500 mg/kg during premating and mating. Reduced body weight and body weight gain was also noted in females treated at 500 mg/kg on Days 14 to 20 post-coitum and during lactation (not always statistically significant).

Food consumption

Food consumption before or after allowance for body weight was reduced during lactation in females treated at 500 mg/kg (statistically not significant).

Other changes in food consumption were considered to be of no toxicological relevance.

Functional observations

No effects were noted at functional observations.

Results on the motor activity test will be added in the draft report.

Haematology

A slight increase in red blood cell distribution width was noted in males at 500 mg/kg. A decrease in eosinophils was noted in females at 500 mg/kg.

Other findings achieving statistical significance (increased APTT in males at 50 and 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Clinical biochemistry

Treatment related effects were mainly noted in males treated at 500 mg/kg. These findings comprised high alanine aminotransferase and aspartate aminotransferase activities (also noted in females at 500 mg/kg) and increased ALP and cholesterol levels. Cholesterol levels were also increased in males treated at 150 mg/kg, but to a lesser extent.

Furthermore, calcium levels were increased in males and females at 500 mg/kg.

Other findings achieving statistical significance (decreased potassium levels in males at 50 mg/kg and increased albumin in females at 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Macroscopic examination

Pale discolouration of the liver was noted in five males treated at 500 mg/kg. No other treatment related effects were noted.

One female at 50 mg/kg (Female 51) showed an enlarged cervix and uterus. The uterus was filled with fluid. These are signs of pseudo pregnancy. These findings were considered to be unrelated to treatment.

Incidental findings among control and treated animals included an enlarged adrenal gland, pelvic dilation of the kidney, reduced size of the seminal vesicles, bent tail apex (correlating to the broken tail apex noted at clinical observations), alopecia, foci on the lungs and diaphragmatic hernia of the liver. These findings are occasionally seen among rats used in these types of study and/or in the absence of a dose response relationship they were considered changes of no toxicological significance.

Organ weights

Liver/body weight ratios were increased with statistical significance for males treated at 500 mg/kg. In addition, thymus/body weight ratios were decreased with statistical significance for males and females treated at 500 mg/kg.

Other changes in organ weight comprised decreased spleen weight in males and females at 500 mg/kg (not always statistically significant), increased heart weight in males at 50, 150 and 500 mg/kg and females at 500 mg/kg, decreased epididymides weight in males at 500 mg/kg, increased relative brain weight in males at 500 mg/kg, increased kidney weight in females at 500 mg/kg and increased adrenal weight in females at 150 and 500 mg/kg.

Other changes (increased liver weight in females at 50 mg/kg, decreased testes weight in males at 50 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Maternal reproduction data

No effect was noted on the duration of gestation and precoital time at 50, 150 or 500 mg/kg.

Five females were non-pregnant (one in the control group, one in the low dose group and three in the high dose group).

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of all pups. One female at 500 mg/kg (Female 79) showed total litter loss.

Erroneously, one female treated at 50 mg/kg (Female 55) was sacrificed before the end of gestation. This female was found to be pregnant. Details will be added in the report.

Litter size/viability of pups

At the first litter check, the average and total number of living pups per litter was reduced at 500 mg/kg (average of 6.9 pups per litter) when compared to concurrent controls (average of 16.0 pups per litter).

Increased postnatal loss was noted at 150 and 500 mg/kg, resulting in a reduced viability index. At 150 mg/kg, postnatal loss was noted in animals 62 (1 of 14 pups), 63 (2 of 20 pups), 67 (1 of 17 pups), 68 (4 of 17 pups) and 69 (2 of 18 pups). At 500 mg/kg, postnatal loss was noted in animals 78 (8 of 11 pups) and 79 (5 of 5 pups).

Increased postnatal loss was also noted at 50 mg/kg. This was mainly due to one animal (Female 60) who cannibalized the pups (in total 13 pups). This was considered to be unrelated to treatment, as no such behaviour was noted in mid and high dose group.

Sex ratios

No treatment related effect on the sex ratio was noted.

Foetal body weight

No treatment related effect on body weights of fetuses was noted.

Please note: For a proper evaluation all in-life data and pathology data are required, therefore the above mentioned findings are preliminary and indicative.

For Public Disclosure

ATTACHMENT 3

Draft Sub-chronic Toxicity Reproductive/Developmental Data on 1,2-Diaminocyclohexane

FOR PUBLIC DISCLOSURE

STATUS REPORT

(End of Treatment)

Study Title

**A COMBINED 28-DAY REPEATED DOSE TOXICITY STUDY WITH
THE REPRODUCTION/DEVELOPMENTAL TOXICITY
SCREENING TEST OF [REDACTED] IN RATS
BY ORAL GAVAGE**

Author

[REDACTED]

Test Facility

[REDACTED]

Laboratory Study Identification

[REDACTED]

FOR PUBLIC DISCLOSURE

INTRODUCTION

Dose Level

- Group 1: 0 mg/kg body weight (Milli-U water)
Group 2: 50 mg/kg body weight
Group 3: 150 mg/kg body weight
Group 4: 500 mg/kg body weight

The purpose of this study was to evaluate the potential toxic effects of the test substance when administered to rats for a minimum of 28 days and to evaluate the potential of the test substance to affect male and female reproductive performance such as gonadal function, mating behaviour, conception, parturition and early postnatal development.

MATERIALS AND METHODS

Allocation

Group	Dose level mg/kg b.w./day	Number of animals		Animals numbers	
		F ₀ males	F ₀ females	males	females
1	0	10	10	01-10	41-50
2	50	10	10	11-20	51-60
3	150	10	10	21-30	61-70
4	500	10	10	31-40	71-80

RESULTS

Mortality

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of the pups. One female at 500 mg/kg (Female 79) was sacrificed due to litter loss on Day 2 of lactation. This animal had five pups, three pups were found dead on Day 1 of lactation, two other pups were found dead on Day 2 of lactation.

Clinical signs

Slight to moderate salivation was noted in all males and females treated at 500 mg/kg. Furthermore, incidentally rales was noted in two males at 500 mg/kg (Males 37 and 38) and piloerection was noted in one female at 500 mg/kg (Female 79) at the end of treatment.

Yellow discolouration of the urine was noted in all animals of Groups 2, 3 and 4 in a dose dependant manner.

Other clinical signs (scabs, chromodacryorrhoea, broken tail apex, diarrhoea and alopecia) were considered unrelated to treatment.

Body weight

Reduced body weight gain was noted in males treated at 500 mg/kg during premating and mating. Reduced body weight and body weight gain was also noted in females treated at 500 mg/kg on Days 14 to 20 post-coitum and during lactation (not always statistically significant).

Food consumption

Food consumption before or after allowance for body weight was reduced during lactation in females treated at 500 mg/kg (statistically not significant).

Other changes in food consumption were considered to be of no toxicological relevance.

Functional observations

No effects were noted at functional observations.

Results on the motor activity test will be added in the draft report.

Haematology

A slight increase in red blood cell distribution width was noted in males at 500 mg/kg. A decrease in eosinophils was noted in females at 500 mg/kg. No concurrent findings were noted, therefore the toxicological relevance of these findings was doubted.

Other findings achieving statistical significance (increased APTT in males at 50 and 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Clinical biochemistry

Treatment related effects were mainly noted in males treated at 500 mg/kg. These findings comprised high alanine aminotransferase and aspartate aminotransferase activities (also noted in females at 500 mg/kg) and increased ALP and cholesterol levels. Cholesterol levels were also increased in males treated at 150 mg/kg, but to a lesser extent.

Furthermore, calcium levels were increased in males and females at 500 mg/kg.

Other findings achieving statistical significance (decreased potassium levels in males at 50 mg/kg and increased albumin in females at 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Macroscopic examination

Pale discolouration of the liver was noted in five males treated at 500 mg/kg. No other treatment related effects were noted.

One female at 50 mg/kg (Female 51) showed an enlarged cervix and uterus. The uterus was filled with fluid. These are signs of pseudo pregnancy. These findings were considered to be unrelated to treatment.

Incidental findings among control and treated animals included an enlarged adrenal gland, pelvic dilation of the kidney, reduced size of the seminal vesicles, bent tail apex (correlating to the broken tail apex noted at clinical observations), alopecia, foci on the lungs and diaphragmatic hernia of the liver. These findings are occasionally seen among rats used in these types of study and/or in the absence of a dose response relationship they were considered changes of no toxicological significance.

Organ weights

Liver/body weight ratios were increased with statistical significance for males treated at 500 mg/kg. In addition, thymus/body weight ratios were decreased with statistical significance for males and females treated at 500 mg/kg.

Other changes in organ weight comprised decreased spleen weight in males and females at 500 mg/kg (not always statistically significant), increased kidney weight in females at 500 mg/kg, increased heart weight in males at 50, 150 and 500 mg/kg and females at 500 mg/kg, decreased epididymides weight in males at 500 mg/kg, increased relative brain weight in males at 500 mg/kg and increased adrenal weight in females at 150 and 500 mg/kg.

Other changes (increased liver weight in females at 50 mg/kg, decreased testes weight in males at 50 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

FOR PUBLIC DISCLOSURE

Maternal reproduction data

No effect was noted on the duration of gestation and precoital time at 50, 150 or 500 mg/kg.

Five females were non-pregnant (one in the control group, one in the low dose group and three in the high dose group).

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of all pups. One female at 500 mg/kg (Female 79) showed total litter loss.

Erroneously, one female treated at 50 mg/kg (Female 55) was sacrificed before the end of gestation. This female was found to be pregnant and showed 13 normally developing implantations (six in the left uterus horn and seven in the right uterus horn), with crown-rump lengths ranging from 2.3 to 2.6 cm.

Litter size/viability of pups

At the first litter check, the average and total number of living pups per litter was reduced at 500 mg/kg (average of 6.9 pups per litter) when compared to concurrent controls (average of 16.0 pups per litter).

Increased postnatal loss was noted at 150 and 500 mg/kg, resulting in a reduced viability index. At 150 mg/kg, postnatal loss was noted in animals 62 (1 of 14 pups), 63 (2 of 20 pups), 67 (1 of 17 pups), 68 (4 of 17 pups) and 69 (2 of 18 pups). At 500 mg/kg, postnatal loss was noted in animals 78 (8 of 11 pups) and 79 (5 of 5 pups).

Increased postnatal loss was also noted at 50 mg/kg. This was mainly due to one animal (Female 60) who cannibalized the pups (in total 13 pups). This was considered to be unrelated to treatment, as no such behaviour was noted in mid and high dose group.

Sex ratios

No treatment related effect on the sex ratio was noted.

Foetal body weight

No treatment related effect on body weights of fetuses was noted.

Please note: For a proper evaluation all in-life data and pathology data are required, therefore the above mentioned findings are preliminary and indicative.

FOR PUBLIC DISCLOSURE

**APPENDIX 1
SUMMARY TABLES**

APPENDIX 1

CLINICAL SIGNS SUMMARY MALES

SIGN (MAX. GRADE) (LOCATION)	PRE MATING		MATING PERIOD	
	WEEK: 1.....	1.....	4.....	
DAY:	123456712345671234567123456712345671234567123			
GROUP 1 (CONTROL)				
Skin / fur / plumage				
Scabs (3)	G:	1111111.....	
(Ear right)	%:	1111111.....	
Secretion / excretion				
Chromodacryorrhoea (3)	G:	1	
(Eye right)	%:	1	
Various				
Broken (1)	G: 1111111111111111	1111111111111111	
(Tail apex)	%: 1111111111111111	1111111111111111	
GROUP 2 (50 MG/KG)				
Skin / fur / plumage				
Yellow discolouration (1)	G:	1111111111111111	
(Urine)	%:	AAAAAAA.....	
Various				
Broken (1)	G: 1111111111111111	1111111111111111	
(Tail apex)	%: 1111111111111111	1111111111111111	
GROUP 3 (150 MG/KG)				
Skin / fur / plumage				
Yellow discolouration (1)	G:	1111111111111111	
(Urine)	%:	AAAAAAA.....	
Secretion / excretion				
Diarrhoea (1)	G:	1.....	
%:	1.....	
GROUP 4 (500 MG/KG)				
Breathing				
Rales (3)	G:	11.....	
%:	11.....	
Skin / fur / plumage				
Yellow discolouration (1)	G: 1111111111111111	1111111111111111	
(Urine)	%: AAAAAAAA.....	AAAAAAA.....	
Secretion / excretion				
Salivation (3)	G:	1. 1111111111111111	
%:	1. 34444.....	AAAAAAA.....	

FEMALES

SIGN (MAX. GRADE) (LOCATION)	PRE MATING	MATING PERIOD
	WEEK: 1.....	1.....
	DAY: 123456712345671234567123456712345671234567123	4.....
GROUP 1 (CONTROL)		
Skin / fur / plumage		
Alopecia (3) (Chest)	G:	1..
Alopecia (3) (Foreleg right)	G:	1..
Alopecia (3) (Hindleg right)	G:	1..
Alopecia (3) (Forelegs)	G:	111111222222..
Alopecia (3) (Hindlegs)	G:	1111111111111111..

G: Median value of the highest individual daily grades

%: Percent of affected animals (0=less than 5%, 1=between 5% and 15%,..., A=more than 95%)

.. Observation performed, sign not present

APPENDIX 1

CLINICAL SIGNS SUMMARY FEMALES

G: Median value of the highest individual daily grades

%: Percent of affected animals (0=less than 5%, 1=between 5% and 15%,..., A=more than 95%)

.. Observation performed, sign not present

APPENDIX 1

**BODY WEIGHTS (GRAM) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAY 1	MEAN	335	335	338	339
WEEK 1	ST.DEV	11.7	9.5	9.0	11.0
	N	10	10	10	10
DAY 8	MEAN	372	366	372	360
WEEK 2	ST.DEV	14.7	12.2	11.5	14.4
	N	10	10	10	10
MATING PERIOD					
DAY 1	MEAN	404	401	401	397
WEEK 1	ST.DEV	17.2	16.9	21.3	16.4
	N	10	10	10	10
DAY 8	MEAN	427	419	419	402 *
WEEK 2	ST.DEV	20.1	20.5	27.8	18.6
	N	10	10	10	10
DAY 15	MEAN	448	438	442	430
WEEK 3	ST.DEV	26.0	22.1	32.3	17.6
	N	10	10	10	10

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAY 1	MEAN	228	230	229	229
WEEK 1	ST.DEV	7.7	7.8	11.2	10.1
	N	10	10	10	10
DAY 8	MEAN	239	239	236	237
WEEK 2	ST.DEV	9.1	5.7	12.4	8.9
	N	10	10	10	10
MATING PERIOD					
DAY 1	MEAN	247	246	246	246
WEEK 1	ST.DEV	8.4	13.9	15.5	10.0
	N	10	10	10	10
DAY 8	MEAN	276	278		265
WEEK 2	ST.DEV	13.7	12.1		0.0
	N	3	3		2
DAY 15	MEAN	293	294		282
WEEK 3	ST.DEV	19.0	28.2		19.8
	N	3	3		2
DAY 22	MEAN	346	348		316
WEEK 4	ST.DEV	55.4	61.8		29.0
	N	3	3		2
DAY 29	MEAN	292	332		296
WEEK 5	ST.DEV	---	41.0		---
	N	1	2		1

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**BODY WEIGHTS (GRAM) SUMMARY
FEMALES
F0-GENERATION**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
POST COITUM					
DAY 0	MEAN	250	251	248	251
	ST.DEV.	13.3	10.4	14.8	8.0
	N	7	7	10	8
DAY 4	MEAN	271	274	265	266
	ST.DEV.	9.5	15.7	15.5	13.6
	N	7	7	10	8
DAY 7	MEAN	282	283	273	278
	ST.DEV.	10.8	17.1	14.2	16.5
	N	7	7	10	8
DAY 11	MEAN	302	305	293	300
	ST.DEV.	14.0	18.2	21.9	19.1
	N	7	7	10	8
DAY 14	MEAN	321	325	312	308
	ST.DEV.	12.7	20.4	21.5	20.7
	N	7	7	10	8
DAY 17	MEAN	363	367	352	331 *
	ST.DEV.	16.1	25.2	22.3	18.2
	N	7	7	10	8
DAY 20	MEAN	418	418	409	361 **
	ST.DEV.	20.0	36.9	27.0	22.7
	N	7	7	10	8
LACTATION					
DAY 1	MEAN	306	324	301	296
	ST.DEV.	15.6	26.2	24.4	18.2
	N	9	8	10	7
DAY 4	MEAN	320	328	314	302
	ST.DEV.	11.7	19.1	22.1	16.6
	N	9	7	10	7

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

APPENDIX 1

**BODY WEIGHT GAIN (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	10	10	10	10
DAY 8	MEAN	11	9	10	6 **
WEEK 2	ST.DEV	2.0	2.2	3.7	1.8
	N	10	10	10	10
MATING PERIOD					
DAY 1	MEAN	21	19	19	17
WEEK 1	ST.DEV	4.0	3.4	6.1	3.6
	N	10	10	10	10
DAY 8	MEAN	28	25	24	19 **
WEEK 2	ST.DEV	5.5	5.1	8.0	4.7
	N	10	10	10	10
DAY 15	MEAN	34	31	31	27
WEEK 3	ST.DEV	6.8	5.3	9.5	4.8
	N	10	10	10	10

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAY 1	MEAN	0	0	0	0
WEEK 1	ST.DEV	0.0	0.0	0.0	0.0
	N	10	10	10	10
DAY 8	MEAN	5	4	3	3
WEEK 2	ST.DEV	2.0	3.0	2.4	3.2
	N	10	10	10	10
MATING PERIOD					
DAY 1	MEAN	8	7	8	8
WEEK 1	ST.DEV	4.0	4.6	2.7	5.0
	N	10	10	10	10
DAY 8	MEAN	21	21	16	
WEEK 2	ST.DEV	3.9	2.0	7.2	
	N	3	3	2	
DAY 15	MEAN	29	28	24	
WEEK 3	ST.DEV	7.7	12.3	16.4	
	N	3	3	2	
DAY 22	MEAN	52	52	39	
WEEK 4	ST.DEV	24.4	27.0	21.3	
	N	3	3	2	
DAY 29	MEAN	28	44	24	
WEEK 5	ST.DEV	---	12.1	---	
	N	1	2	1	

/ Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**BODY WEIGHT GAIN (%) SUMMARY
FEMALES
F0-GENERATION**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
POST COITUM					
DAY 0	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	7	7	10	8
DAY 4	MEAN	9	9	7	6
	ST.DEV.	2.7	3.3	2.5	2.7
	N	7	7	10	8
DAY 7	MEAN	13	13	10	11
	ST.DEV.	3.0	3.8	3.6	4.0
	N	7	7	10	8
DAY 11	MEAN	21	22	18	19
	ST.DEV.	3.1	4.8	6.1	5.0
	N	7	7	10	8
DAY 14	MEAN	28	30	26	22
	ST.DEV.	3.2	5.1	5.1	5.2
	N	7	7	10	8
DAY 17	MEAN	45	46	42	32 **
	ST.DEV.	3.3	6.9	4.8	4.9
	N	7	7	10	8
DAY 20	MEAN	67	67	65	44 **
	ST.DEV.	4.8	11.0	7.3	7.2
	N	7	7	10	8
LACTATION					
DAY 1	MEAN	0	0	0	0
	ST.DEV.	0.0	0.0	0.0	0.0
	N	9	8	10	7
DAY 4	MEAN	5	3	4	2
	ST.DEV.	3.7	5.2	4.5	3.5
	N	9	7	10	7

** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAYS 1-8	MEAN	29	28	28	28
WEEKS 1-2	ST.DEV	0.4	0.3	0.4	0.3
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	30	29	30	32 **
WEEKS 2-3	ST.DEV	0.3	0.2	0.1	0.6
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE MATING MEAN		29	29	29	30

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAYS 1-8	MEAN	19	19	19	19
WEEKS 1-2	ST.DEV	0.5	0.6	1.2	1.9
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	20	20	20	22
WEEKS 2-3	ST.DEV	0.1	0.6	0.8	1.3
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE MATING MEAN		20	20	20	21

** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES
F0-GENERATION**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
POST COITUM					
DAYS 0-4	MEAN	24	24	22	25
	ST.DEV.	2.4	3.6	1.6	6.0
	N	7	7	10	8
DAYS 4-7	MEAN	23	23	23	25
	ST.DEV.	1.3	3.3	6.5	4.0
	N	7	7	10	8
DAYS 7-11	MEAN	25	26	24	25
	ST.DEV.	2.9	2.1	2.4	3.3
	N	7	7	10	8
DAYS 11-14	MEAN	28	32	26	29
	ST.DEV.	3.4	6.5	3.1	3.2
	N	7	7	10	8
DAYS 14-17	MEAN	33	32	29 *	31
	ST.DEV.	3.3	1.2	2.4	2.4
	N	7	7	10	8
DAYS 17-20	MEAN	32	34	30	32
	ST.DEV.	2.8	3.5	2.4	3.1
	N	7	7	10	8
MEAN OF MEANS		28	29	26	28
LACTATION					
DAYS 1-4	MEAN	35	40	42	23
	ST.DEV.	5.6	12.3	18.5	5.6
	N	9	7	10	7

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

APPENDIX 1

**RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAYS 1-8	MEAN	78	76	76	79
WEEKS 1-2	ST.DEV	0.3	0.0	0.8	2.3
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	81	80	80	89 **
WEEKS 2-3	ST.DEV	1.7	1.6	0.0	0.2
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE MATING MEAN					
		79	78	78	84

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
PRE MATING					
DAYS 1-8	MEAN	81	81	81	80
WEEKS 1-2	ST.DEV	0.9	3.7	2.9	5.1
	N (CAGE)	2	2	2	2
DAYS 8-15	MEAN	83	84	85	93 *
WEEKS 2-3	ST.DEV	1.7	3.7	1.3	2.1
	N (CAGE)	2	2	2	2
MEAN OF MEANS OVER PRE MATING MEAN					
		82	82	83	87

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY) SUMMARY
FEMALES
F0-GENERATION**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
POST COITUM					
DAYS 0-4	MEAN	88	87	83	95
	ST.DEV.	7.4	8.5	5.3	20.5
	N	7	7	10	8
DAYS 4-7	MEAN	83	83	86	89
	ST.DEV.	4.2	7.2	26.5	10.6
	N	7	7	10	8
DAYS 7-11	MEAN	83	86	82	84
	ST.DEV.	7.9	7.3	4.7	8.2
	N	7	7	10	8
DAYS 11-14	MEAN	88	101	84	94
	ST.DEV.	9.4	23.3	5.1	7.3
	N	7	7	10	8
DAYS 14-17	MEAN	90	88	82	94
	ST.DEV.	9.4	4.8	6.5	7.7
	N	7	7	10	8
DAYS 17-20	MEAN	77	82	74	88 **
	ST.DEV.	4.6	7.1	5.1	7.5
	N	7	7	10	8
MEAN OF MEANS		85	88	82	91
LACTATION					
DAYS 1-4	MEAN	108	121	135	75
	ST.DEV.	15.2	31.4	56.0	17.5
	N	9	7	10	7

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level
Explanations for excluded data are listed in the tables of the individual values

APPENDIX 1

**FUNCTIONAL OBSERVATIONS SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
TREATMENT					
HEARING SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 5
PUPIL L SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 5
PUPIL R SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 5
STATIC R SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 5
GRIP SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 5

FEMALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
TREATMENT					
HEARING SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 6
PUPIL L SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 6
PUPIL R SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 6
STATIC R SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 6
GRIP SCORE 0/1	MEDIAN N	0 5	0 5	0 5	0 6

+//+ Steel-test significant at 5% (+) or 1% (++) level

APPENDIX 1

HAEMATOLOGY SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
WBC 10E9/l	MEAN ST.DEV N	9.8 1.7 5	10.2 1.9 5	9.0 1.0 5	10.6 1.1 5
Neutrophils %WBC	MEAN ST.DEV N	17.3 6.1 5	13.1 2.4 5	13.0 1.0 5	17.4 6.3 5
Lymphocytes %WBC	MEAN ST.DEV N	76.8 7.2 5	83.3 2.5 5	82.4 2.0 5	78.4 6.4 5
Monocytes %WBC	MEAN ST.DEV N	3.9 1.4 5	2.1 0.6 5	2.9 1.2 5	3.5 2.1 5
Eosinophils %WBC	MEAN ST.DEV N	1.6 0.5 5	1.2 0.1 5	1.3 0.5 5	0.4 + 0.3 5
Basophils %WBC	MEAN ST.DEV N	0.4 0.3 5	0.5 0.1 5	0.4 0.1 5	0.3 0.2 5
Red blood cells 10E12/l	MEAN ST.DEV N	8.40 0.15 5	8.30 0.24 5	8.52 0.39 5	8.12 0.28 5
Reticulocytes	MEAN %RBC ST.DEV N	2.9 0.6 5	3.1 0.4 5	3.1 0.4 5	3.4 0.4 5
RDW	MEAN % ST.DEV N	11.8 0.4 5	12.6 0.6 5	12.7 0.7 5	13.0 *
Haemoglobin mmol/l	MEAN ST.DEV N	9.7 0.3 5	9.5 0.5 5	9.6 0.1 5	9.5 0.3 5
Haematocrit l/l	MEAN ST.DEV N	0.439 0.019 5	0.424 0.022 5	0.431 0.009 5	0.422 0.012 5
MCV	MEAN fl ST.DEV N	52.2 2.5 5	51.1 2.3 5	50.6 2.2 5	52.0 1.7 5
MCH	MEAN fmol ST.DEV N	1.15 0.04 5	1.15 0.06 5	1.13 0.05 5	1.17 0.05 5
MCHC	MEAN mmol/l ST.DEV N	22.14 0.28 5	22.44 0.28 5	22.26 0.31 5	22.47 0.30 5
Platelets	MEAN 10E9/l ST.DEV N	901 215 5	1056 120 5	1025 88 5	981 245 5
PT	MEAN s ST.DEV N	18.2 0.8 5	17.5 0.6 5	18.0 0.6 5	18.0 0.8 5
APTT	MEAN s ST.DEV N	11.7 1.6 5	17.3 ** 1.2 5	15.7 * 3.0 5	15.0 2.6 5

+/** Steel-test significant at 5% (+) or 1% (++) level

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**HAEMATOLOGY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
WBC	MEAN	7.3	5.0	5.0	5.8
10E9/l	ST.DEV	2.5	1.5	1.5	1.4
	N	5	5	5	5
Neutrophils	MEAN	19.2	21.5	23.1	27.5
%WBC	ST.DEV	4.1	5.5	5.1	12.1
	N	5	5	5	5
Lymphocytes	MEAN	77.4	74.6	73.3	68.9
%WBC	ST.DEV	4.0	6.3	5.7	12.4
	N	5	5	5	5
Monocytes	MEAN	2.2	2.7	2.6	3.0
%WBC	ST.DEV	0.5	1.4	0.7	0.6
	N	5	5	5	5
Eosinophils	MEAN	1.0	1.1	0.7	0.3 +
%WBC	ST.DEV	0.4	1.2	0.3	0.2
	N	5	5	5	5
Basophils	MEAN	0.3	0.1	0.2	0.3
%WBC	ST.DEV	0.1	0.2	0.1	0.1
	N	5	5	5	5
Red blood cells	MEAN	7.62	7.49	7.49	7.39
10E12/l	ST.DEV	0.27	0.39	0.42	0.73
	N	5	5	5	5
Reticulocytes	MEAN	6.0	5.6	6.9	6.0
%RBC	ST.DEV	2.3	1.0	2.5	2.3
	N	5	5	5	5
RDW	MEAN	15.0	16.1	15.5	15.3
%	ST.DEV	1.7	1.6	1.7	1.9
	N	5	5	5	5
Haemoglobin	MEAN	9.1	8.9	9.0	8.8
mmol/l	ST.DEV	0.6	0.4	0.5	0.6
	N	5	5	5	5
Haematocrit	MEAN	0.409	0.401	0.409	0.397
l/l	ST.DEV	0.018	0.017	0.021	0.022
	N	5	5	5	5
MCV	MEAN	53.7	53.6	54.7	54.0
f ¹	ST.DEV	0.9	3.0	2.0	2.6
	N	5	5	5	5
MCH	MEAN	1.20	1.20	1.20	1.20
fmol	ST.DEV	0.04	0.06	0.03	0.05
	N	5	5	5	5
MCHC	MEAN	22.34	22.33	21.88	22.25
mmol/l	ST.DEV	0.49	0.42	0.35	0.50
	N	5	5	5	5
Platelets	MEAN	1342	1200	1439	1317
10E9/l	ST.DEV	196	315	385	233
	N	5	5	5	5
PT	MEAN	17.4	16.8	17.3	18.0
s	ST.DEV	0.3	0.9	0.8	1.4
	N	5	5	5	5
APTT	MEAN	18.0	16.8	16.6	17.5
s	ST.DEV	1.4	3.5	2.7	3.7
	N	5	5	5	5

+/++ Steel-test significant at 5% (+) or 1% (++) level

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**CLINICAL BIOCHEMISTRY SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
ALAT U/l	MEAN	37.5	38.4	45.9	65.5 **
	ST.DEV	4.5	7.8	11.6	3.0
	N	5	5	5	5
ASAT U/l	MEAN	73.9	71.7	78.8	96.5 **
	ST.DEV	5.9	4.8	6.7	8.1
	N	5	5	5	5
ALP U/l	MEAN	103	111	113	149 **
	ST.DEV	25	7	11	22
	N	5	5	5	5
Total protein g/l	MEAN	62.3	62.8	63.4	63.1
	ST.DEV	2.2	3.0	2.9	3.0
	N	5	5	5	5
Albumin g/l	MEAN	31.0	31.0	31.2	31.4
	ST.DEV	0.9	0.7	1.2	1.4
	N	5	5	5	5
Total bilirubin umol/l	MEAN	2.4	2.6	2.6	2.8
	ST.DEV	0.2	0.4	0.3	0.3
	N	5	5	5	5
Urea mmol/l	MEAN	6.2	5.8	6.0	6.9
	ST.DEV	0.6	0.9	1.1	0.4
	N	5	5	5	5
Creatinine umol/l	MEAN	39.0	38.5	37.5	39.0
	ST.DEV	2.2	0.8	1.8	2.0
	N	5	5	5	5
Glucose mmol/l	MEAN	8.06	8.72	8.35	9.00
	ST.DEV	0.66	1.12	1.59	1.17
	N	5	5	5	5
Cholesterol mmol/l	MEAN	1.52	1.88	2.04 **	2.49 **
	ST.DEV	0.23	0.34	0.19	0.17
	N	5	5	5	5
Sodium mmol/l	MEAN	142.4	142.6	141.5	141.7
	ST.DEV	0.7	1.1	0.8	0.6
	N	5	5	5	5
Potassium mmol/l	MEAN	4.26	3.77 **	4.05	4.03
	ST.DEV	0.25	0.18	0.09	0.17
	N	5	5	5	5
Chloride mmol/l	MEAN	103	103	103	103
	ST.DEV	1	1	1	1
	N	5	5	5	5
Calcium mmol/l	MEAN	2.75	2.70	2.81	2.92 **
	ST.DEV	0.05	0.07	0.06	0.07
	N	5	5	5	5
Inorg.Phos mmol/l	MEAN	2.54	2.20	2.33	2.69
	ST.DEV	0.20	0.25	0.18	0.19
	N	5	5	5	5

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**CLINICAL BIOCHEMISTRY SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
ALAT U/l	MEAN ST.DEV N	58.1 5.7 5	57.9 12.7 5	50.6 4.1 5	65.0 12.8 5
ASAT U/l	MEAN ST.DEV N	75.2 7.3 5	74.3 12.9 5	71.7 7.3 5	96.0 * 11.5 5
ALP U/l	MEAN ST.DEV N	78 17 5	91 21 5	86 48 5	70 19 5
Total protein g/l	MEAN ST.DEV N	62.8 2.3 5	64.4 2.9 5	64.3 1.6 5	61.5 1.2 5
Albumin g/l	MEAN ST.DEV N	30.6 0.6 5	31.3 1.1 5	32.2 * 0.9 5	31.7 0.6 5
Total bilirubin umol/l	MEAN ST.DEV N	2.6 0.2 5	2.3 0.3 5	3.0 0.5 5	3.0 0.7 5
Urea mmol/l	MEAN ST.DEV N	7.5 0.5 5	7.3 1.0 5	6.5 1.4 5	7.0 0.5 5
Creatinine umol/l	MEAN ST.DEV N	42.9 2.5 5	42.3 4.2 5	43.9 1.8 5	42.0 2.0 5
Glucose mmol/l	MEAN ST.DEV N	7.54 1.15 5	7.04 1.16 5	7.40 1.32 5	7.04 0.45 5
Cholesterol mmol/l	MEAN ST.DEV N	1.55 0.13 5	1.56 0.38 5	1.42 0.32 5	1.27 0.29 5
Sodium mmol/l	MEAN ST.DEV N	137.8 1.1 5	138.3 1.5 5	137.6 1.4 5	137.2 1.3 5
Potassium mmol/l	MEAN ST.DEV N	3.78 0.27 5	3.66 0.65 5	3.31 0.39 5	3.85 0.12 5
Chloride mmol/l	MEAN ST.DEV N	100 1 5	99 1 5	98 2 5	100 1 5
Calcium mmol/l	MEAN ST.DEV N	2.58 0.06 5	2.58 0.05 5	2.63 0.08 5	2.73 ** 0.08 5
Inorg.Phos mmol/l	MEAN ST.DEV N	1.87 0.20 5	2.00 0.26 5	1.96 0.28 5	2.11 0.30 5

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**MACROSCOPIC FINDINGS SUMMARY
MALES**

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT				
Animals examined	10	10	10	10
Animals without findings	8	8	9	5
Animals affected	2	2	1	5
Liver				
Discolouration	0	0	0	5 #
Kidneys				
Pelvic dilation	1	0	0	0
Seminal vesicles				
Reduced in size	0	1	1	0
Bone				
Tail apex: bent.	1	1	0	0

FEMALES

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
INTERCURRENT DEATH				
Animals examined	1		1	
Animals without findings	0		1	
Animals affected	1		0	
Stomach				
Contents:	1		0	
END OF TREATMENT				
Animals examined	10	9	10	9
Animals without findings	10	6	9	8
Animals affected	0	3	1	1
Lungs				
Focus/foci	0	0	0	1
Liver				
Diaphragmatic hernia	0	0	1	0
Uterus				
Enlarged	0	1	0	0
Contains fluid	0	1	0	0
Cervix				
Enlarged	0	1	0	0
Adrenal glands				
Enlarged	0	1	0	0
Skin				
Alopecia	0	1	0	0

/ ## Fisher's Exact test significant at 5% (#) or 1% (##) level

APPENDIX 1

ORGAN WEIGHTS (GRAM) SUMMARY
MALES

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	424	416	416	403
	ST.DEV	24	24	33	15
	N	10	10	10	10
BRAIN (GRAM)	MEAN	2.04	2.14	2.09	2.09
	ST.DEV	0.10	0.07	0.11	0.03
	N	5	5	5	5
HEART (GRAM)	MEAN	1.263	1.322	1.348	1.416 *
	ST.DEV	0.077	0.070	0.133	0.032
	N	5	5	5	5
LIVER (GRAM)	MEAN	11.47	10.42	10.93	12.46
	ST.DEV	1.18	0.36	1.53	0.59
	N	5	5	5	5
THYMUS (GRAM)	MEAN	0.467	0.362	0.379	0.285 *
	ST.DEV	0.113	0.066	0.120	0.043
	N	5	5	5	5
KIDNEYS (GRAM)	MEAN	3.15	3.13	3.09	3.15
	ST.DEV	0.26	0.25	0.33	0.21
	N	5	5	5	5
ADRENALS (GRAM)	MEAN	0.067	0.070	0.070	0.078
	ST.DEV	0.014	0.011	0.009	0.010
	N	5	5	5	5
SPLEEN (GRAM)	MEAN	1.080	0.924	1.023	0.889
	ST.DEV	0.186	0.106	0.154	0.078
	N	5	5	5	5
TESTES (GRAM)	MEAN	4.04	3.69 *	3.84	4.00
	ST.DEV	0.29	0.29	0.28	0.30
	N	10	10	10	10
EPIDIDYMIDES (GRAM)	MEAN	1.250	1.227	1.169	1.036 **
	ST.DEV	0.122	0.095	0.051	0.094
	N	10	10	10	10

*//** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
MALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	424	416	416	403
	ST.DEV	24	24	33	15
	N	10	10	10	10
BRAIN (%)	MEAN	0.47	0.52	0.50	0.53 *
	ST.DEV	0.02	0.03	0.05	0.02
	N	5	5	5	5
HEART (%)	MEAN	0.292	0.324 *	0.322 *	0.355 **
	ST.DEV	0.017	0.023	0.011	0.017
	N	5	5	5	5
LIVER (%)	MEAN	2.65	2.55	2.60	3.13 **
	ST.DEV	0.16	0.10	0.18	0.23
	N	5	5	5	5
THYMUS (%)	MEAN	0.108	0.086	0.089	0.072 *
	ST.DEV	0.023	0.018	0.022	0.011
	N	5	5	5	5
KIDNEYS (%)	MEAN	0.73	0.77	0.74	0.79
	ST.DEV	0.06	0.06	0.05	0.04
	N	5	5	5	5
ADRENALS (%)	MEAN	0.016	0.017	0.017	0.020
	ST.DEV	0.003	0.002	0.003	0.002
	N	5	5	5	5
SPLEEN (%)	MEAN	0.249	0.227	0.243	0.223
	ST.DEV	0.038	0.031	0.018	0.015
	N	5	5	5	5
TESTES (%)	MEAN	0.96	0.89	0.93	0.99
	ST.DEV	0.09	0.08	0.07	0.06
	N	10	10	10	10
EPIDIDYMIDES (%)	MEAN	0.296	0.295	0.282	0.257 **
	ST.DEV	0.036	0.025	0.016	0.023
	N	10	10	10	10

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**ORGAN WEIGHTS (GRAM) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	268	286	283	271
	ST.DEV	14	13	14	17
	N	5	5	5	5
BRAIN (GRAM)	MEAN	1.91	1.91	1.89	1.84
	ST.DEV	0.06	0.06	0.08	0.06
	N	5	5	5	5
HEART (GRAM)	MEAN	0.950	1.005	1.013	1.049 *
	ST.DEV	0.059	0.061	0.053	0.065
	N	5	5	5	5
LIVER (GRAM)	MEAN	9.22	10.23 *	9.85	9.27
	ST.DEV	0.38	0.41	0.76	0.58
	N	5	5	5	5
THYMUS (GRAM)	MEAN	0.228	0.226	0.201	0.158 *
	ST.DEV	0.048	0.058	0.016	0.027
	N	5	5	5	5
KIDNEYS (GRAM)	MEAN	2.01	2.15	2.26	2.37 **
	ST.DEV	0.15	0.19	0.11	0.18
	N	5	5	5	5
ADRENALS (GRAM)	MEAN	0.093	0.108	0.114 *	0.113 *
	ST.DEV	0.008	0.014	0.009	0.008
	N	5	5	5	5
SPLEEN (GRAM)	MEAN	0.885	0.876	0.870	0.691
	ST.DEV	0.040	0.105	0.213	0.118
	N	5	5	5	5

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**ORGAN/BODY WEIGHT RATIOS (%) SUMMARY
FEMALES**

		GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
END OF TREATMENT					
BODY W. (GRAM)	MEAN	268	286	283	271
	ST.DEV	14	13	14	17
	N	5	5	5	5
BRAIN (%)	MEAN	0.71	0.67	0.67	0.68
	ST.DEV	0.06	0.03	0.02	0.03
	N	5	5	5	5
HEART (%)	MEAN	0.355	0.353	0.358	0.388
	ST.DEV	0.026	0.027	0.027	0.028
	N	5	5	5	5
LIVER (%)	MEAN	3.45	3.58	3.48	3.43
	ST.DEV	0.25	0.04	0.31	0.24
	N	5	5	5	5
THYMUS (%)	MEAN	0.085	0.079	0.071	0.058 *
	ST.DEV	0.016	0.018	0.005	0.009
	N	5	5	5	5
KIDNEYS (%)	MEAN	0.75	0.75	0.80	0.88 *
	ST.DEV	0.07	0.07	0.03	0.04
	N	5	5	5	5
ADRENALS (%)	MEAN	0.035	0.038	0.040	0.042
	ST.DEV	0.004	0.004	0.004	0.006
	N	5	5	5	5
SPLEEN (%)	MEAN	0.331	0.306	0.309	0.255
	ST.DEV	0.030	0.025	0.083	0.033
	N	5	5	5	5

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

APPENDIX 1

**MATING PERFORMANCE
F0-GENERATION - POST COITUM**

DAY OF THE PAIRING PERIOD	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
NUMBER OF FEMALES MATED DURING THE FIRST PAIRING PERIOD				
1	1	3	4	1
2	1	-	-	3
3	3	1	3	3
4	2	3	2	1
5	-	-	1	-
MEDIAN PRECOITAL TIME	3	3	3	3
MEAN PRECOITAL TIME	2.9	2.6	2.6	2.5
N	7	7	10	8

+/++ Steel-test significant at 5% (+) or 1% (++) level

APPENDIX 1

**BREEDING DATA PER GROUP
F0-GENERATION - LACTATION**

	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
LITTERS TOTAL	9	8	10	7
DURATION OF GESTATION				
MEAN (+)	21.2	21.5	21.2	21.9
ST.DEV.	0.8	0.5	0.6	0.4
N	9	8	10	7
DEAD PUPS AT FIRST LITTER CHECK				
LITTERS AFFECTED (#)	2	1	1	1
TOTAL	2	1	3	3
MEAN (+)	0.2	0.1	0.3	0.4
ST.DEV.	0.4	0.4	0.9	1.1
N	9	8	10	7
LIVING PUPS AT FIRST LITTER CHECK				
% OF MALES / FEMALES (#)	45 / 55	43 / 58	49 / 51	48 / 52
TOTAL	144	120	167	48
MEAN (+)	16.0	15.0	16.7	6.9 ++
ST.DEV.	1.7	3.6	2.0	3.0
N	9	8	10	7
POSTNATAL LOSS				
% OF LIVING PUPS	0.0	11.7	4.8	16.7
LITTERS AFFECTED (#)	0	2	3	1
TOTAL (#)	0	14 ##	8 ##	8 ##
MEAN (+)	0.0	1.8	0.8	1.1
ST.DEV.	0.0	4.6	1.4	3.0
N	9	8	10	7
CULLED PUPS				
TOTAL	0	0	0	0
LIVING PUPS DAY . P.P.				
TOTAL	144	105	158	38
MEAN (+)	16.0	13.1	15.8	5.4 ++
ST.DEV.	1.7	6.4	1.9	3.2
N	9	8	10	7
BREEDING LOSS DAYS , - , P.P.				
% OF LIVING PUPS AT DAY . P.P.	0.0	0.0	0.6	0.0
LITTERS AFFECTED (#)	0	0	1	0
TOTAL (#)	0	0	1	0
MEAN (+)	0.0	0.0	0.1	0.0
ST.DEV.	0.0	0.0	0.3	0.0
N	9	8	10	7
LIVING PUPS DAY . P.P.				
% OF MALES / FEMALES (#)	0 / 0	0 / 0	0 / 0	0 / 0
TOTAL	0	0	0	0
MEAN (+)	0.0	0.0	0.0	0.0
ST.DEV.	0.0	0.0	0.0	0.0
N	9	8	10	7
VIABILITY INDEX (#)	100.0	87.5 ##	94.6 ##	79.2 ##
WEANING INDEX (#)	0.0	0.0	0.0	0.0

Viability index = (Number of alive pups on day 4 p.p. / Number of pups born alive) *100
 Weaning index =(Number of alive pups on day 21 p.p. / Number of alive pups on day 4 p.p.) *100
 +/- Steel-test significant at 5% (+) or 1% (++) level
 # / ## Fisher's Exact test significant at 5% (#) or 1% (##) level

APPENDIX 1

**MEAN BODY WEIGHTS OF PUPS PER GROUP (GRAM)
F0-GENERATION - LACTATION**

DAY	SEX	GROUP 1 CONTROL	GROUP 2 50 MG/KG	GROUP 3 150 MG/KG	GROUP 4 500 MG/KG
1	M	MEAN	6.6	6.7	6.6
		ST.DEV.	0.5	0.6	0.8
		N	9	8	7
	F	MEAN	6.2	6.5	6.3
		ST.DEV.	0.6	0.7	0.7
		N	9	8	7
	M+F	MEAN	6.4	6.6	6.4
		ST.DEV.	0.5	0.6	0.6
		N	9	8	7
4	M	MEAN	9.5	10.2	9.1
		ST.DEV.	1.1	1.4	0.8
		N	9	7	10
	F	MEAN	8.9	9.5	8.3
		ST.DEV.	1.3	1.7	0.8
		N	9	7	10
	M+F	MEAN	9.2	9.8	8.7
		ST.DEV.	1.2	1.5	0.8
		N	9	7	10

*/** Dunnett-test based on pooled variance significant at 5% (*) or 1% (**) level

FOR PUBLIC DISCLOSURE

**APPENDIX 2
INDIVIDUAL TABLES**

APPENDIX 2

**MORTALITY DATA
MALES**

ANIMAL SCHEDULED NECROPSY	OTHER	TREATMENT FROM	TO
GROUP 1 (CONTROL)			
1 08FEB07		08JAN07	07FEB07
2 08FEB07		08JAN07	07FEB07
3 08FEB07		08JAN07	07FEB07
4 08FEB07		08JAN07	07FEB07
5 08FEB07		08JAN07	07FEB07
6 08FEB07		08JAN07	07FEB07
7 08FEB07		08JAN07	07FEB07
8 08FEB07		08JAN07	07FEB07
9 08FEB07		08JAN07	07FEB07
10 08FEB07		08JAN07	07FEB07
GROUP 2 (50 MG/KG)			
11 08FEB07		08JAN07	07FEB07
12 08FEB07		08JAN07	07FEB07
13 08FEB07		08JAN07	07FEB07
14 08FEB07		08JAN07	07FEB07
15 08FEB07		08JAN07	07FEB07
16 08FEB07		08JAN07	07FEB07
17 08FEB07		08JAN07	07FEB07
18 08FEB07		08JAN07	07FEB07
19 08FEB07		08JAN07	07FEB07
20 08FEB07		08JAN07	07FEB07
GROUP 3 (150 MG/KG)			
21 08FEB07		08JAN07	07FEB07
22 08FEB07		08JAN07	07FEB07
23 08FEB07		08JAN07	07FEB07
24 08FEB07		08JAN07	07FEB07
25 08FEB07		08JAN07	07FEB07
26 08FEB07		08JAN07	07FEB07
27 08FEB07		08JAN07	07FEB07
28 08FEB07		08JAN07	07FEB07
29 08FEB07		08JAN07	07FEB07
30 08FEB07		08JAN07	07FEB07
GROUP 4 (500 MG/KG)			
31 08FEB07		08JAN07	07FEB07
32 08FEB07		08JAN07	07FEB07
33 08FEB07		08JAN07	07FEB07
34 08FEB07		08JAN07	07FEB07
35 08FEB07		08JAN07	07FEB07
36 08FEB07		08JAN07	07FEB07
37 08FEB07		08JAN07	07FEB07
38 08FEB07		08JAN07	07FEB07
39 08FEB07		08JAN07	07FEB07
40 08FEB07		08JAN07	07FEB07

APPENDIX 2

**MORTALITY DATA
FEMALES**

ANIMAL	SCHEDULED NECROPSY	OTHER	TREATMENT FROM	TO
GROUP 1 (CONTROL)				
41	22FEB07		08JAN07	21FEB07
42	21FEB07		08JAN07	20FEB07
43	19FEB07		08JAN07	18FEB07
44	20FEB07		08JAN07	19FEB07
45	20FEB07		08JAN07	19FEB07
46	19FEB07		08JAN07	18FEB07
47	20FEB07		08JAN07	19FEB07
48	20FEB07		08JAN07	19FEB07
49	21FEB07		08JAN07	20FEB07
50	21FEB07		08JAN07	21FEB07
GROUP 2 (50 MG/KG)				
51	21FEB07		08JAN07	21FEB07
52	22FEB07		08JAN07	21FEB07
53	19FEB07		08JAN07	18FEB07
54	20FEB07		08JAN07	19FEB07
55	21FEB07		08JAN07	21FEB07
56	22FEB07		08JAN07	21FEB07
57	22FEB07		08JAN07	21FEB07
58	19FEB07		08JAN07	18FEB07
59	20FEB07		08JAN07	19FEB07
60		15FEB07	08JAN07	15FEB07
GROUP 3 (150 MG/KG)				
61	22FEB07		08JAN07	21FEB07
62	19FEB07		08JAN07	18FEB07
63	21FEB07		08JAN07	20FEB07
64	19FEB07		08JAN07	18FEB07
65	19FEB07		08JAN07	18FEB07
66	21FEB07		08JAN07	20FEB07
67	21FEB07		08JAN07	20FEB07
68	21FEB07		08JAN07	20FEB07
69	19FEB07		08JAN07	18FEB07
70	20FEB07		08JAN07	19FEB07
GROUP 4 (500 MG/KG)				
71	21FEB07		08JAN07	20FEB07
72	20FEB07		08JAN07	19FEB07
73	21FEB07		08JAN07	21FEB07
74	21FEB07		08JAN07	20FEB07
75	21FEB07		08JAN07	21FEB07
76	21FEB07		08JAN07	20FEB07
77	21FEB07		08JAN07	21FEB07
78	20FEB07		08JAN07	19FEB07
79		17FEB07	08JAN07	17FEB07
80	20FEB07		08JAN07	19FEB07

APPENDIX 2

CLINICAL SIGNS MALES

G: Highest daily grades

C. Highest daily grades
:: Observation performed, sign not present

APPENDIX 2

**CLINICAL SIGNS
MALES**

SIGN (MAX. GRADE) (LOCATION)	PRE MATING	MATING PERIOD	
		WEEK: 1.....	1.....
			4.....
GROUP 2 (50 MG/KG)			
ANIMAL 18			
Skin / fur / plumage			
Yellow discolouration (1)	G:	111111111111111111	
(Urine)			
ANIMAL 19			
Skin / fur / plumage			
Yellow discolouration (1)	G:	111111111111111111	
(Urine)			
ANIMAL 20			
Skin / fur / plumage			
Yellow discolouration (1)	G:	111111111111111111	
(Urine)			
GROUP 3 (150 MG/KG)			
ANIMAL 21			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 22			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
Secretion / excretion			
Diarrhoea (1)	G:1.....		
ANIMAL 23			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 24			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 25			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 26			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 27			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 28			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 29			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			
ANIMAL 30			
Skin / fur / plumage			
Yellow discolouration (1)	G: ...111111111111111111	111111111111111111	
(Urine)			

G: Highest daily grades

..: Observation performed, sign not present

APPENDIX 2

CLINICAL SIGNS MALES

G: Highest daily grades
∴ Observation performed, sign not present

APPENDIX 2

CLINICAL SIGNS MALES

G: Highest daily grades
∴ Observation performed, sign not present

APPENDIX 2

CLINICAL SIGNS FEMALES

G: Highest daily grades

G. Highest daily grades
:: Observation performed, sign not present

APPENDIX 2

CLINICAL SIGNS FEMALES

G: Highest daily grades
.. Observation performed, sign not present

APPENDIX 2

CLINICAL SIGNS FEMALES

G: Highest daily grades
.. Observation performed, sign not present

APPENDIX 2

**BODY WEIGHTS (GRAM)
MALES**

ANIMAL	PRE MATING		MATING PERIOD						
	DAYS	WEEKS	1	8	1	8	15	22	29
GROUP 1 (CONTROL)									
1	334	376			420	445	471		
2	329	359			395	413	434		
3	333	380			418	447	474		
4	327	362			396	419	431		
5	331	369			395	428	445		
6	340	382			414	441	458		
7	333	377			419	445	477		
8	326	360			382	404	413		
9	328	353			377	389	405		
10	366	403			425	440	467		
GROUP 2 (50 MG/KG)									
11	344	372			423	451	471		
12	338	363			405	418	429		
13	333	367			388	409	428		
14	331	362			405	429	439		
15	327	349			381	389	402		
16	335	357			387	393	421		
17	352	378			407	420	444		
18	321	355			379	410	428		
19	328	363			402	419	448		
20	345	391			429	449	474		
GROUP 3 (150 MG/KG)									
21	327	362			394	412	434		
22	342	384			427	453	486		
23	347	357			371	378	397		
24	349	368			388	403	421		
25	343	383			431	462	492		
26	341	371			397	408	429		
27	338	388			423	445	478		
28	341	374			411	432	446		
29	327	374			385	398	424		
30	323	354			378	395	417		
GROUP 4 (500 MG/KG)									
31	349	366			406	402	433		
32	351	373			405	408	433		
33	328	350			389	419	449		
34	327	340			383	395	421		
35	335	350			377	374	410		
36	326	346			374	389	413		
37	349	365			393	403	423		
38	339	361			420	406	437		
39	332	360			402	384	417		
40	355	389			420	440	467		

APPENDIX 2

**BODY WEIGHTS (GRAM)
FEMALES**

DAYS WEEKS	PRE MATING			MATING PERIOD				ANIMAL
	1 1	8 2	1 2	8 3	15 4	22 5	29 6	
GROUP 1 (CONTROL)								
41	239	251	254	---	---	---	---	
42	239	244	237	---	---	---	---	
43	231	240	254	288	312	387	---	
44	220	230	230	---	---	---	---	
45	223	242	248	261	292	368	---	
46	218	224	242	---	---	---	---	
47	221	230	248	---	---	---	---	
48	234	252	258	---	---	---	---	
49	226	236	247	---	---	---	---	
50	228	242	248	279	274	283	292	
GROUP 2 (50 MG/KG)								
51	223	241	229	265	273	306	303	
52	234	239	240	---	---	---	---	
53	241	242	259	---	---	---	---	
54	220	236	244	---	---	---	---	
55	236	248	244	289	283	319	361	
56	216	229	224	---	---	---	---	
57	233	244	241	---	---	---	---	
58	231	232	247	---	---	---	---	
59	229	241	260	280	326	419	---	
60	235	235	269	---	---	---	---	
GROUP 3 (150 MG/KG)								
61	212	218	218					
62	240	241	264					
63	240	247	255					
64	228	230	249					
65	218	223	232					
66	229	237	239					
67	224	235	247					
68	219	233	240					
69	233	232	248					
70	246	262	272					
GROUP 4 (500 MG/KG)								
71	237	253	257	---	---	---	---	
72	224	234	252	---	---	---	---	
73	238	240	243	265	268	295	296	
74	238	250	259	---	---	---	---	
75	229	234	233	---	---	---	---	
76	230	234	233	---	---	---	---	
77	245	236	258	---	---	---	---	
78	221	225	237	---	---	---	---	
79	218	231	244	265	296	336	---	
80	214	228	248	---	---	---	---	

APPENDIX 2

**BODY WEIGHTS (GRAM)
FEMALES
F0-GENERATION**

DAYS	POST COITUM							LACTATION	
	0	4	7	11	14	17	20	1	4
ANIMAL									
GROUP 1 (CONTROL)									
41	271	289	304	330	341	387	454	332	333
42	239	260	273	298	310	357	418	292	302
43	—	—	—	—	—	—	—	307	330
44	241	265	280	291	323	357	401	284	303
45	—	—	—	—	—	—	—	306	313
46	238	269	274	296	309	352	410	307	331
47	250	270	276	295	312	351	403	303	320
48	266	278	287	310	335	386	437	327	325
49	246	269	282	292	317	352	405	294	324
GROUP 2 (50 MG/KG)									
52	257	281	286	298	323	365	415	321	329
53	258	299	313	338	363	412	473	374	350
54	247	265	276	291	317	367	425	313	326
56	235	255	266	288	306	327	348	298	293
57	251	264	275	306	315	366	418	303	332
58	241	264	269	295	310	355	416	305	318
59	—	—	—	—	—	—	—	330	347
60	265	287	299	321	342	374	432	350	---
GROUP 3 (150 MG/KG)									
61	230	245	258	273	287	329	380	265	278
62	250	279	282	305	316	347	396	332	328
63	251	275	282	303	330	362	427	300	315
64	243	263	282	312	322	356	429	306	339
65	231	241	248	244	270	309	357	273	276
66	248	263	269	295	314	368	418	304	323
67	261	271	276	308	325	370	424	338	326
68	240	254	273	288	315	353	417	290	313
69	246	265	264	281	296	340	392	282	306
70	281	292	298	316	342	387	447	322	338
GROUP 4 (500 MG/KG)									
71	248	272	292	307	314	338	354	291	308
72	258	278	291	327	332	355	386	312	307
74	264	286	300	316	336	355	398	322	323
75 <NP>	253	266	275	287	297	312	327	—	—
76	244	251	260	276	282	308	343	278	294
77 <NP>	253	271	283	306	319	334	356	—	—
78	238	246	253	273	284	316	357	270	273
79	—	—	—	—	—	—	—	301	295
80	251	258	270	304	298	330	368	300	316

<NP> Non-pregnant

APPENDIX 2

**BODY WEIGHT GAIN (%)
MALES**

ANIMAL	PRE MATING		MATING PERIOD					
	DAYS	WEEKS	1	8	15	22	29	36
1	0	13	26	33	41			
2	0	9	20	26	32			
3	0	14	26	34	42			
4	0	11	21	28	32			
5	0	11	19	29	34			
6	0	12	22	30	35			
7	0	13	26	34	43			
8	0	10	17	24	27			
9	0	8	15	19	23			
10	0	10	16	20	28			
GROUP 1 (CONTROL)								
11	0	8	23	31	37			
12	0	7	20	24	27			
13	0	10	17	23	29			
14	0	9	22	30	33			
15	0	7	17	19	23			
16	0	7	16	17	26			
17	0	7	16	19	26			
18	0	11	18	28	33			
19	0	11	23	28	37			
20	0	13	24	30	37			
GROUP 2 (50 MG/KG)								
21	0	11	20	26	33			
22	0	12	25	32	42			
23	0	3	7	9	14			
24	0	5	11	15	21			
25	0	12	26	35	43			
26	0	9	16	20	26			
27	0	15	25	32	41			
28	0	10	21	27	31			
29	0	14	18	22	30			
30	0	10	17	22	29			
GROUP 3 (150 MG/KG)								
31	0	5	16	15	24			
32	0	6	15	16	23			
33	0	7	19	28	37			
34	0	4	17	21	29			
35	0	4	13	12	22			
36	0	6	15	19	27			
37	0	5	13	15	21			
38	0	6	24	20	29			
39	0	8	21	16	26			
40	0	10	18	24	32			
GROUP 4 (500 MG/KG)								

APPENDIX 2

**BODY WEIGHT GAIN (%)
FEMALES**

ANIMAL	PRE MATING						MATING PERIOD			
	DAYS		1	8	1	8	15	22	29	36
	WEEKS		1	2	1	2	3	4	5	6
GROUP 1 (CONTROL)										
41	0	5	6	—	—	—	—	—	—	
42	0	2	-1	—	—	—	—	—	—	
43	0	4	10	25	35	68	—	—	—	
44	0	5	5	—	—	—	—	—	—	
45	0	9	11	17	31	65	—	—	—	
46	0	3	11	—	—	—	—	—	—	
47	0	4	12	—	—	—	—	—	—	
48	0	8	10	—	—	—	—	—	—	
49	0	4	9	—	—	—	—	—	—	
50	0	6	9	22	20	24	28	—	—	
GROUP 2 (50 MG/KG)										
51	0	8	3	19	22	37	36	—	—	
52	0	2	3	—	—	—	—	—	—	
53	0	0	7	—	—	—	—	—	—	
54	0	7	11	—	—	—	—	—	—	
55	0	5	3	22	20	35	53	—	—	
56	0	6	4	—	—	—	—	—	—	
57	0	5	3	—	—	—	—	—	—	
58	0	0	7	—	—	—	—	—	—	
59	0	5	14	22	42	83	—	—	—	
60	0	0	14	—	—	—	—	—	—	
GROUP 3 (150 MG/KG)										
61	0	3	3	—	—	—	—	—	—	
62	0	0	10	—	—	—	—	—	—	
63	0	3	6	—	—	—	—	—	—	
64	0	1	9	—	—	—	—	—	—	
65	0	3	7	—	—	—	—	—	—	
66	0	3	4	—	—	—	—	—	—	
67	0	5	10	—	—	—	—	—	—	
68	0	6	10	—	—	—	—	—	—	
69	0	0	6	—	—	—	—	—	—	
70	0	7	11	—	—	—	—	—	—	
GROUP 4 (500 MG/KG)										
71	0	7	8	—	—	—	—	—	—	
72	0	4	13	—	—	—	—	—	—	
73	0	1	2	11	13	24	24	—	—	
74	0	5	9	—	—	—	—	—	—	
75	0	2	2	—	—	—	—	—	—	
76	0	2	1	—	—	—	—	—	—	
77	0	-4	5	—	—	—	—	—	—	
78	0	2	7	—	—	—	—	—	—	
79	0	6	12	22	36	54	—	—	—	
80	0	7	16	—	—	—	—	—	—	

APPENDIX 2

**BODY WEIGHT GAIN (%)
FEMALES
F0-GENERATION**

DAYS ANIMAL	POST COITUM							LACTATION		
	0	4	7	11	14	17	20	1	4	
GROUP 1 (CONTROL)										
41	0	7	12	22	26	43	68	0	0	
42	0	9	14	25	30	49	75	0	3	
43	—	—	—	—	—	—	—	0	7	
44	0	10	16	21	34	48	66	0	7	
45	—	—	—	—	—	—	—	0	2	
46	0	13	15	24	30	48	72	0	8	
47	0	8	10	18	25	40	61	0	6	
48	0	5	8	17	26	45	64	0	-1	
49	0	9	15	19	29	43	65	0	10	
GROUP 2 (50 MG/KG)										
52	0	9	11	16	26	42	61	0	2	
53	0	16	21	31	41	60	83	0	-6	
54	0	7	12	18	28	49	72	0	4	
56	0	9	13	23	30	39	48	0	-2	
57	0	5	10	22	25	46	67	0	10	
58	0	10	12	22	29	47	73	0	4	
59	—	—	—	—	—	—	—	0	5	
60	0	8	13	21	29	41	63	0	—	
GROUP 3 (150 MG/KG)										
61	0	7	12	19	25	43	65	0	5	
62	0	12	13	22	26	39	58	0	-1	
63	0	10	12	21	31	44	70	0	5	
64	0	8	16	28	33	47	77	0	11	
65	0	4	7	6	17	34	55	0	1	
66	0	6	8	19	27	48	69	0	6	
67	0	4	6	18	25	42	62	0	-4	
68	0	6	14	20	31	47	74	0	8	
69	0	8	7	14	20	38	59	0	9	
70	0	4	6	12	22	38	59	0	5	
GROUP 4 (500 MG/KG)										
71	0	10	18	24	27	36	43	0	6	
72	0	8	13	27	29	38	50	0	-2	
74	0	8	14	20	27	34	51	0	0	
75 <NP>	0	5	9	13	17	23	29	—	—	
76	0	3	7	13	16	26	41	0	6	
77 <NP>	0	7	12	21	26	32	41	—	—	
78	0	3	6	15	19	33	50	0	1	
79	—	—	—	—	—	—	—	0	-2	
80	0	3	8	21	19	31	47	0	5	

<NP> Non-pregnant

APPENDIX 2

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

PRE MATING		
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		

GROUP 1 (CONTROL)

1	29	30
2	29	30

GROUP 2 (50 MG/KG)

3	28	29
4	28	29

GROUP 3 (150 MG/KG)

5	28	30
6	29	30

GROUP 4 (500 MG/KG)

7	29	32
8	28	33

FEMALES

PRE MATING		
DAYS	1-8	8-15
WEEKS	1-2	2-3
CAGE		

GROUP 1 (CONTROL)

9	20	20
10	19	20

GROUP 2 (50 MG/KG)

11	19	20
12	20	20

GROUP 3 (150 MG/KG)

13	18	19
14	20	21

GROUP 4 (500 MG/KG)

15	20	23
16	18	21

APPENDIX 2

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES
F0-GENERATION

DAYS ANIMAL	POST COITUM						LACTATION	
	0-4	4-7	7-11	11-14	14-17	17-20	1-4	
GROUP 1 (CONTROL)								
41	28	25	30	31	34	37	39	
42	21	22	29	26	39	31	28	
43	—	—	—	—	—	—	37	
44	25	23	24	34	31	31	33	
45	—	—	—	—	—	—	29	
46	25	24	22	23	33	35	44	
47	26	23	24	29	31	29	40	
48	22	22	24	27	32	33	30	
49	23	24	24	28	28	29	31	
GROUP 2 (50 MG/KG)								
52	24	24	28	30	31	36	44	
53	29	29	29	28	34	33	55	
54	24	22	26	37	31	34	34	
56	20	21	27	29	32	29	28	
57	20	19	27	27	32	33	38	
58	22	22	23	45	32	36	25	
59	—	—	—	—	—	—	56	
60	28	26	24	31	34	40	—	
GROUP 3 (150 MG/KG)								
61	21	41	23	23	26	26	35	
62	25	22	23	24	29	30	78	
63	22	21	25	30	26	29	31	
64	23	25	27	27	29	34	69	
65	21	20	20	22	25	28	46	
66	20	18	25	27	32	29	29	
67	21	21	27	27	30	33	27	
68	21	22	25	27	29	32	27	
69	24	22	21	23	32	29	52	
70	23	21	25	31	28	30	29	
GROUP 4 (500 MG/KG)								
71	22	26	27	28	31	29	19	
72	28	30	28	35	34	32	22	
74	25	29	28	32	29	38	20	
75 <NP>	26	28	27	28	33	32	—	
76	19	20	23	25	27	31	23	
77 <NP>	38	22	23	27	31	32	—	
78	20	21	19	27	30	27	15	
79	—	—	—	—	—	—	29	
80	24	23	28	31	33	32	31	

<NP> Non-pregnant

APPENDIX 2

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
MALES

PRE MATING
DAYS 1-8 8-15
WEEKS 1-2 2-3
CAGE

GROUP 1 (CONTROL)

1 77 82
2 78 79

GROUP 2 (50 MG/KG)

3 76 81
4 76 79

GROUP 3 (150 MG/KG)

5 76 80
6 77 80

GROUP 4 (500 MG/KG)

7 80 89
8 77 89

FEMALES

PRE MATING
DAYS 1-8 8-15
WEEKS 1-2 2-3
CAGE

GROUP 1 (CONTROL)

9 82 82
10 81 84

GROUP 2 (50 MG/KG)

11 78 81
12 83 86

GROUP 3 (150 MG/KG)

13 79 84
14 83 86

GROUP 4 (500 MG/KG)

15 84 95
16 77 92

APPENDIX 2

RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)
FEMALES
F0-GENERATION

DAYS ANIMAL	POST COITUM						LACTATION
	0-4	4-7	7-11	11-14	14-17	17-20	1-4
GROUP 1 (CONTROL)							
41	95	83	89	90	89	81	118
42	81	81	98	84	108	75	94
43	---	---	---	---	---	---	111
44	92	83	81	104	87	78	110
45	---	---	---	---	---	---	94
46	93	89	75	74	93	85	132
47	96	83	81	93	89	73	126
48	78	75	77	82	82	76	92
49	84	86	83	87	80	72	95
GROUP 2 (50 MG/KG)							
52	86	84	92	94	85	86	133
53	98	94	85	77	83	70	156
54	92	80	88	116	85	79	104
56	79	80	94	95	98	82	96
57	76	70	89	86	88	79	115
58	81	83	76	146	89	87	78
59	---	---	---	---	---	---	162
60	96	87	76	91	90	93	---
GROUP 3 (150 MG/KG)							
61	85	159	82	80	79	69	127
62	88	77	74	77	84	77	238
63	78	76	83	92	73	67	98
64	87	87	87	84	81	80	203
65	87	81	81	81	82	79	165
66	76	67	83	87	88	69	89
67	76	76	87	83	81	78	83
68	84	82	88	86	82	77	87
69	91	82	76	79	95	74	170
70	80	69	78	92	73	68	86
GROUP 4 (500 MG/KG)							
71	79	89	87	88	92	81	61
72	100	102	86	104	97	83	71
74	88	98	89	95	81	95	62
75 <NP>	96	103	93	93	107	99	---
76	77	77	84	90	89	90	79
77 <NP>	141	78	76	85	92	90	---
78	82	82	69	95	95	76	55
79	---	---	---	---	---	---	98
80	93	85	90	105	99	88	97

<NP> Non-pregnant

APPENDIX 2

FUNCTIONAL OBSERVATIONS
MALES
TREATMENT

ANIMAL	HEARING	PUPIL L	PUPIL R	STATIC R	GRIP
	SCORE 0/1				

GROUP 1 (CONTROL)

1	0	0	0	0	0
2	0	0	0	0	0
4	0	0	0	0	0
6	0	0	0	0	0
7	0	0	0	0	0

GROUP 2 (50 MG/KG)

12	0	0	0	0	0
13	0	0	0	0	0
14	0	0	0	0	0
16	0	0	0	0	0
17	0	0	0	0	0

GROUP 3 (150 MG/KG)

21	0	0	0	0	0
22	0	0	0	0	0
23	0	0	0	0	0
24	0	0	0	0	0
25	0	0	0	0	0

GROUP 4 (500 MG/KG)

31	0	0	0	0	0
32	0	0	0	0	0
34	0	0	0	0	0
35	0	0	0	0	0
36	0	0	0	0	0

FEMALES
TREATMENT

ANIMAL	HEARING	PUPIL L	PUPIL R	STATIC R	GRIP
	SCORE 0/1				

GROUP 1 (CONTROL)

42	0	0	0	0	0
44	0	0	0	0	0
45	0	0	0	0	0
47	0	0	0	0	0
48	0	0	0	0	0

GROUP 2 (50 MG/KG)

52	0	0	0	0	0
53	0	0	0	0	0
54	0	0	0	0	0
58	0	0	0	0	0
59	0	0	0	0	0

GROUP 3 (150 MG/KG)

62	0	0	0	0	0
63	0	0	0	0	0
64	0	0	0	0	0
66	0	0	0	0	0
70	0	0	0	0	0

APPENDIX 2

FUNCTIONAL OBSERVATIONS
FEMALES
TREATMENT

ANIMAL	HEARING	PUPIL L	PUPIL R	STATIC R	GRIP
	SCORE 0/1				

GROUP 4 (500 MG/KG)

71	0	0	0	0	0
72	0	0	0	0	0
74	0	0	0	0	0
78	0	0	0	0	0
79	0	0	0	0	0
80	0	0	0	0	0

APPENDIX 2

HAEMATOLOGY
MALES
END OF TREATMENT

ANIMAL	WBC 10E9/l	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
1	6.8	20.6	72.4	4.7	1.6
2	10.7	16.0	78.0	5.0	1.0
4	10.1	10.4	85.1	1.8	2.1
6	10.6	26.0	67.0	5.0	2.0
7	11.0	13.5	81.4	3.2	1.3
GROUP 2 (50 MG/KG)					
12	7.8	15.6	79.9	2.8	1.1
13	9.7	13.1	83.7	1.5	1.2
14	9.4	15.1	81.9	1.4	1.1
16	11.7	9.7	86.5	2.3	1.2
17	12.6	11.8	84.4	2.3	1.2
GROUP 3 (150 MG/KG)					
21	8.7	12.0	85.0	1.7	0.9
22	7.6	13.8	81.1	2.5	2.1
23	8.8	11.9	83.8	2.6	1.4
24	10.2	13.9	81.8	2.8	1.1
25	9.8	13.4	80.1	4.8	1.1
GROUP 4 (500 MG/KG)					
31	10.6	14.7	82.7	1.9	0.3
32	10.3	17.0	78.2	3.6	0.7
34	9.1	14.0	83.4	1.7	0.5
35	12.3	28.3	67.6	3.3	0.4
36	10.7	13.0	80.0	7.0	0.0

MALES
END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/l	Reticulocytes %RBC	RDW %	Haemoglobin mmol/l
GROUP 1 (CONTROL)					
1	0.7	8.20	2.9	11.6	9.5
2	0.0	8.61	2.5	12.0	9.4
4	0.5	8.40	2.6	12.3	9.8
6	0.0	8.39	2.5	11.3	9.6
7	0.6	8.42	4.0	12.0	10.2
GROUP 2 (50 MG/KG)					
12	0.6	8.63	2.8	12.3	9.9
13	0.5	7.97	3.8	12.8	9.3
14	0.6	8.36	3.1	13.0	9.3
16	0.3	8.26	3.0	11.6	10.2
17	0.4	8.30	2.8	13.1	8.9
GROUP 3 (150 MG/KG)					
21	0.4	8.45	3.3	12.3	9.7
22	0.5	8.15	3.6	12.1	9.5
23	0.2	9.05	2.4	12.8	9.7
24	0.5	8.78	3.2	13.9	9.4
25	0.5	8.19	3.2	12.2	9.5

APPENDIX 2

HAEMATOLOGY
MALES
END OF TREATMENT

ANIMAL	Basophils %WBC	Red blood cells 10E12/l	Reticulocytes %RBC	RDW %	Haemoglobin mmol/l
GROUP 4 (500 MG/KG)					
31	0.3	8.20	3.6	13.5	9.6
32	0.4	7.87	2.8	12.2	9.2
34	0.4	7.80	3.9	13.7	9.5
35	0.3	8.49	3.3	13.4	9.3
36	0.0	8.22	3.3	12.3	9.9

MALES
END OF TREATMENT

ANIMAL	Haematocrit l/l	MCV fl	MCH fmol	MCHC mmol/l	Platelets 10E9/l
GROUP 1 (CONTROL)					
1	0.425	51.8	1.16	22.39	1048
2	0.420	48.8	1.09	22.42	747
4	0.443	52.8	1.17	22.17	1127
6	0.437	52.1	1.14	21.93	612
7	0.469	55.7	1.21	21.78	972
GROUP 2 (50 MG/KG)					
12	0.447	51.8	1.14	22.08	1034
13	0.410	51.5	1.17	22.71	904
14	0.419	50.2	1.12	22.29	1174
16	0.447	54.1	1.23	22.73	986
17	0.398	47.9	1.07	22.40	1180
GROUP 3 (150 MG/KG)					
21	0.433	51.2	1.15	22.48	1046
22	0.433	53.0	1.17	21.97	1039
23	0.443	49.0	1.07	21.90	1043
24	0.418	47.6	1.07	22.59	1119
25	0.426	52.1	1.17	22.38	879
GROUP 4 (500 MG/KG)					
31	0.420	51.2	1.17	22.78	789
32	0.408	51.8	1.17	22.50	1310
34	0.418	53.6	1.21	22.62	1047
35	0.423	49.8	1.09	21.98	1062
36	0.442	53.7	1.21	22.45	686

MALES
END OF TREATMENT

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
1	17.6	11.5
2	17.8	11.5
4	19.7	14.3
6	17.9	11.1
7	18.2	10.1

APPENDIX 2

HAEMATOLOGY
MALES
END OF TREATMENT

ANIMAL	PT S	APTT S
GROUP 2 (50 MG/KG)		
12	16.9	17.1
13	18.4	19.0
14	17.6	18.0
16	17.0	16.0
17	17.7	16.4
GROUP 3 (150 MG/KG)		
21	17.4	11.5
22	18.5	19.1
23	18.6	16.7
24	17.9	17.3
25	17.4	13.8
GROUP 4 (500 MG/KG)		
31	18.6	16.1
32	17.7	15.2
34	18.6	17.4
35	18.2	15.6
36	16.8	10.6

FEMALES
END OF TREATMENT

ANIMAL	WBC 10E9/l	Neutrophils %WBC	Lymphocytes %WBC	Monocytes %WBC	Eosinophils %WBC
GROUP 1 (CONTROL)					
42	3.7	21.6	75.7	2.1	0.4
44	6.8	18.5	77.4	2.7	1.0
45	7.4	24.7	72.3	1.9	0.9
47	10.8	16.9	78.5	2.7	1.4
48	7.6	14.1	83.1	1.5	1.1
GROUP 2 (50 MG/KG)					
52	5.5	18.0	79.0	3.0	0.0
53	3.5	31.0	64.0	5.0	0.0
54	6.4	20.2	76.6	1.5	1.5
58	3.3	21.0	74.0	2.0	3.0
59	6.3	17.2	79.4	2.1	0.9
GROUP 3 (150 MG/KG)					
62	5.1	22.5	74.5	2.4	0.4
63	5.6	30.6	65.0	3.5	0.5
64	2.4	24.4	72.0	2.1	1.2
66	5.8	21.7	74.2	3.1	0.6
70	6.3	16.4	80.9	1.7	0.8
GROUP 4 (500 MG/KG)					
71	5.2	19.6	77.6	2.1	0.3
72	7.8	22.8	73.6	3.1	0.3
74	6.5	46.5	49.5	3.0	0.7
78	4.3	31.8	64.1	3.7	0.2
80	5.0	16.6	79.7	3.3	0.2

APPENDIX 2

**HAEMATOLOGY
FEMALES
END OF TREATMENT**

ANIMAL	Basophils %WBC	Red blood cells 10E12/l	Reticulocytes %RBC	RDW %	Haemoglobin mmol/l
GROUP 1 (CONTROL)					
42	0.3	7.24	9.8	17.9	8.2
44	0.4	7.81	5.0	14.6	9.6
45	0.2	7.58	6.2	14.8	9.3
47	0.5	7.95	4.7	14.6	9.6
48	0.2	7.53	4.1	13.3	9.0
GROUP 2 (50 MG/KG)					
52	0.0	7.84	4.3	14.8	8.9
53	0.0	8.00	5.3	16.1	9.3
54	0.2	7.18	5.3	14.8	8.6
58	0.0	7.20	6.9	18.8	8.4
59	0.4	7.25	6.4	16.0	9.4
GROUP 3 (150 MG/KG)					
62	0.2	7.74	4.8	14.5	9.1
63	0.3	7.14	10.5	17.5	8.7
64	0.3	7.05	7.7	17.1	8.6
66	0.3	8.05	7.1	14.3	9.7
70	0.1	7.46	4.2	13.9	8.7
GROUP 4 (500 MG/KG)					
71	0.4	8.03	3.6	12.7	9.4
72	0.2	8.26	3.3	14.0	9.4
74	0.2	6.68	7.3	16.3	8.0
78	0.2	7.22	8.2	17.5	8.8
80	0.3	6.74	7.4	16.0	8.6

**FEMALES
END OF TREATMENT**

ANIMAL	Haematocrit l/l	MCV fl	MCH fmol	MCHC mmol/l	Platelets 10E9/l
GROUP 1 (CONTROL)					
42	0.381	52.6	1.13	21.54	1460
44	0.420	53.8	1.23	22.88	1323
45	0.417	55.0	1.23	22.31	1499
47	0.426	53.6	1.20	22.45	1418
48	0.401	53.3	1.20	22.52	1011
GROUP 2 (50 MG/KG)					
52	0.389	49.7	1.14	22.95	822
53	0.419	52.4	1.17	22.29	1286
54	0.388	54.1	1.20	22.10	1570
58	0.387	53.7	1.17	21.84	1391
59	0.420	57.9	1.30	22.45	930
GROUP 3 (150 MG/KG)					
62	0.412	53.3	1.18	22.15	1016
63	0.402	56.3	1.22	21.60	1364
64	0.400	56.8	1.22	21.51	1285
66	0.444	55.2	1.20	21.81	1472
70	0.388	52.0	1.16	22.32	2058

APPENDIX 2

**HAEMATOLOGY
FEMALES
END OF TREATMENT**

ANIMAL	Haematocrit l/l	MCV fl	MCH fmol	MCHC mmol/l	Platelets 10E9/l
GROUP 4 (500 MG/KG)					
71	0.418	52.1	1.17	22.43	1071
72	0.416	50.3	1.14	22.58	1132
74	0.370	55.4	1.19	21.56	1262
78	0.404	55.9	1.22	21.91	1546
80	0.378	56.1	1.28	22.78	1574

**FEMALES
END OF TREATMENT**

ANIMAL	PT s	APTT s
GROUP 1 (CONTROL)		
42	16.8	17.0
44	17.5	16.7
45	17.7	17.5
47	17.5	20.2
48	17.4	18.6
GROUP 2 (50 MG/KG)		
52	17.8	18.4
53	16.2	14.3
54	17.3	21.8
58	15.6	12.9
59	17.0	16.5
GROUP 3 (150 MG/KG)		
62	17.3	16.1
63	18.6	18.9
64	17.0	19.8
66	16.9	15.0
70	16.5	13.2
GROUP 4 (500 MG/KG)		
71	15.8	13.1
72	18.3	20.1
74	18.7	17.0
78	19.4	22.1
80	18.0	15.0

APPENDIX 2

**CLINICAL BIOCHEMISTRY
MALES
END OF TREATMENT**

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	Total protein g/l	Albumin g/l
GROUP 1 (CONTROL)					
1	31.4	68.1	97	64.4	32.3
2	42.5	83.3	145	62.9	31.0
4	35.6	71.8	84	58.6	29.7
6	36.7	75.2	86	63.5	30.9
7	41.1	70.9	101	62.1	31.0
GROUP 2 (50 MG/KG)					
12	30.3	75.3	112	63.7	32.0
13	34.5	70.8	101	61.3	30.7
14	36.4	65.8	114	66.9	30.9
16	51.0	77.6	120	63.4	31.5
17	39.8	69.0	110	58.7	30.1
GROUP 3 (150 MG/KG)					
21	43.0	73.0	120	61.4	31.0
22	34.9	74.4	98	61.2	30.0
23	64.8	75.8	115	68.3	33.1
24	48.0	89.3	108	63.5	31.4
25	38.8	81.4	125	62.7	30.4
GROUP 4 (500 MG/KG)					
31	64.2	101.1	158	66.2	32.5
32	62.7	92.0	140	61.1	31.5
34	67.2	88.2	123	58.9	29.5
35	69.8	108.3	182	64.0	30.8
36	63.5	92.8	140	65.3	32.9

**MALES
END OF TREATMENT**

ANIMAL	Total bilirubin umol/l	Urea mmol/l	Creatinine umol/l	Glucose mmol/l	Cholesterol mmol/l
GROUP 1 (CONTROL)					
1	2.2	6.6	42.1	7.50	1.84
2	2.5	5.9	38.6	7.25	1.38
4	2.5	6.7	39.3	8.48	1.59
6	2.6	5.3	35.8	8.78	1.56
7	2.3	6.6	39.3	8.29	1.24
GROUP 2 (50 MG/KG)					
12	2.4	5.2	37.2	8.27	1.53
13	2.8	5.8	38.6	9.30	1.65
14	2.3	5.1	38.6	9.44	1.99
16	3.2	7.4	38.6	6.96	2.39
17	2.5	5.6	39.3	9.64	1.83
GROUP 3 (150 MG/KG)					
21	2.6	7.3	40.0	6.23	1.76
22	2.4	5.6	38.6	7.49	2.19
23	2.6	7.0	35.8	9.27	2.23
24	2.2	4.7	36.5	8.39	2.02
25	3.1	5.2	36.5	10.37	2.00

APPENDIX 2

**CLINICAL BIOCHEMISTRY
MALES
END OF TREATMENT**

ANIMAL	Total bilirubin umol/l	Urea mmol/l	Creatinine umol/l	Glucose mmol/l	Cholesterol mmol/l
GROUP 4 (500 MG/KG)					
31	2.8	6.7	38.6	8.19	2.24
32	2.6	6.9	42.1	9.92	2.69
34	2.8	7.1	38.6	7.63	2.59
35	3.2	6.5	36.5	8.85	2.46
36	2.5	7.5	39.3	10.43	2.48

**MALES
END OF TREATMENT**

ANIMAL	Sodium mmol/l	Potassium mmol/l	Chloride mmol/l	Calcium mmol/l	Inorg.Phos mmol/l
GROUP 1 (CONTROL)					
1	141.4	4.11	103	2.80	2.34
2	143.1	3.98	103	2.74	2.44
4	142.5	4.39	104	2.67	2.54
6	142.9	4.19	104	2.79	2.52
7	142.3	4.62	103	2.74	2.86
GROUP 2 (50 MG/KG)					
12	144.2	3.78	105	2.67	2.06
13	142.6	3.72	104	2.67	2.09
14	142.9	3.52	103	2.67	2.03
16	142.2	4.02	102	2.83	2.19
17	141.2	3.82	102	2.65	2.64
GROUP 3 (150 MG/KG)					
21	142.0	4.19	103	2.87	2.55
22	141.2	4.03	103	2.78	2.44
23	141.8	4.07	104	2.86	2.26
24	142.3	3.98	104	2.72	2.07
25	140.4	3.98	102	2.82	2.33
GROUP 4 (500 MG/KG)					
31	141.9	3.80	102	2.93	2.46
32	141.4	3.98	102	2.97	2.57
34	141.8	4.02	102	2.81	2.93
35	140.9	4.26	103	2.91	2.67
36	142.5	4.07	104	3.00	2.83

**FEMALES
END OF TREATMENT**

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	Total protein g/l	Albumin g/l
GROUP 1 (CONTROL)					
42	65.8	87.6	100	61.1	30.1
44	52.8	71.7	83	64.1	31.2
45	62.3	72.8	71	66.1	31.4
47	53.3	68.7	55	62.1	30.5
48	56.2	75.0	82	60.6	30.0

APPENDIX 2

**CLINICAL BIOCHEMISTRY
FEMALES
END OF TREATMENT**

ANIMAL	ALAT U/l	ASAT U/l	ALP U/l	Total protein g/l	Albumin g/l
GROUP 2 (50 MG/KG)					
52	53.8	75.6	84	69.1	32.8
53	65.1	95.1	73	62.4	30.3
54	76.4	62.8	126	62.0	30.2
58	45.5	73.3	96	63.2	31.4
59	48.7	64.5	77	65.5	31.9
GROUP 3 (150 MG/KG)					
62	52.8	67.5	165	61.6	30.6
63	47.7	83.5	68	65.6	32.6
64	51.1	70.9	42	64.4	32.7
66	45.6	72.1	59	65.1	32.4
70	55.9	64.4	95	64.9	32.8
GROUP 4 (500 MG/KG)					
71	64.7	89.9	66	63.5	32.4
72	53.0	94.4	61	60.4	31.5
74	70.5	107.5	90	60.6	30.7
78	53.4	81.0	46	61.7	32.0
80	83.5	107.3	88	61.4	31.7

**FEMALES
END OF TREATMENT**

ANIMAL	Total bilirubin umol/l	Urea mmol/l	Creatinine umol/l	Glucose mmol/l	Cholesterol mmol/l
GROUP 1 (CONTROL)					
42	2.5	7.4	42.7	8.04	1.49
44	2.6	7.4	39.3	6.73	1.37
45	2.6	8.4	41.9	5.94	1.57
47	2.3	7.1	45.3	8.48	1.63
48	2.8	7.1	45.3	8.51	1.70
GROUP 2 (50 MG/KG)					
52	2.5	6.0	38.9	6.15	1.09
53	1.8	7.8	46.4	6.31	2.13
54	2.3	8.4	43.3	6.13	1.67
58	2.3	6.7	37.1	8.06	1.50
59	2.7	7.7	45.9	8.53	1.39
GROUP 3 (150 MG/KG)					
62	2.6	7.9	43.8	7.72	1.69
63	2.7	6.9	46.1	6.70	0.91
64	2.7	6.1	45.1	8.81	1.70
66	3.2	4.2	41.3	8.28	1.35
70	3.7	7.4	43.3	5.49	1.45
GROUP 4 (500 MG/KG)					
71	3.1	6.1	42.7	7.15	1.68
72	4.1	7.0	40.6	7.77	1.14
74	2.1	7.5	43.4	6.65	0.91
78	2.6	7.1	39.3	6.73	1.19
80	3.2	7.2	43.9	6.88	1.43

APPENDIX 2

**CLINICAL BIOCHEMISTRY
FEMALES
END OF TREATMENT**

ANIMAL	Sodium mmol/l	Potassium mmol/l	Chloride mmol/l	Calcium mmol/l	Inorg.Phos mmol/l
GROUP 1 (CONTROL)					
42	138.4	3.81	100	2.50	1.80
44	136.1	4.17	99	2.61	1.76
45	137.7	3.43	101	2.57	2.01
47	137.6	3.80	98	2.65	1.65
48	139.2	3.70	100	2.56	2.14
GROUP 2 (50 MG/KG)					
52	137.0	4.07	99	2.64	1.70
53	140.3	2.52	98	2.51	2.20
54	139.2	3.95	101	2.59	2.33
58	136.8	3.70	98	2.56	1.89
59	138.2	4.05	100	2.58	1.89
GROUP 3 (150 MG/KG)					
62	137.3	3.55	98	2.55	2.37
63	137.3	3.00	97	2.60	1.82
64	139.0	2.80	96	2.60	1.87
66	135.5	3.48	97	2.65	1.66
70	138.8	3.73	101	2.76	2.10
GROUP 4 (500 MG/KG)					
71	136.3	3.89	99	2.81	2.58
72	136.6	3.99	100	2.73	2.05
74	136.4	3.93	101	2.63	2.17
78	139.5	3.70	101	2.82	1.82
80	137.2	3.75	101	2.67	1.91

APPENDIX 2

**MACROSCOPIC FINDINGS
MALES
ALL NECROPSIES**

ANIMAL ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)		
1	No findings noted	Scheduled necropsy, 08Feb2007
2	No findings noted	Scheduled necropsy, 08Feb2007
3	No findings noted	Scheduled necropsy, 08Feb2007
4	No findings noted	Scheduled necropsy, 08Feb2007
5	Kidneys	Right side: pelvic dilation.
6	Bone	Tail apex: bent.
7		No findings noted
8		No findings noted
9		No findings noted
10		No findings noted
GROUP 2 (50 MG/KG)		
11	No findings noted	Scheduled necropsy, 08Feb2007
12	No findings noted	Scheduled necropsy, 08Feb2007
13	No findings noted	Scheduled necropsy, 08Feb2007
14		No findings noted
15	Bone	Tail apex: bent.
16		No findings noted
17		No findings noted
18		No findings noted
19		No findings noted
20	Seminal vesicles	Right side: reduced in size.
GROUP 3 (150 MG/KG)		
21	No findings noted	Scheduled necropsy, 08Feb2007
22	No findings noted	Scheduled necropsy, 08Feb2007
23	No findings noted	Scheduled necropsy, 08Feb2007
24	No findings noted	Scheduled necropsy, 08Feb2007
25	No findings noted	Scheduled necropsy, 08Feb2007
26	No findings noted	Scheduled necropsy, 08Feb2007
27	No findings noted	Scheduled necropsy, 08Feb2007
28	No findings noted	Scheduled necropsy, 08Feb2007
29	No findings noted	Scheduled necropsy, 08Feb2007
30	Seminal vesicles	Left side: reduced in size.
GROUP 4 (500 MG/KG)		
31	Liver	Discolouration, pale.
32		No findings noted
33	Liver	Discolouration, pale.
34		No findings noted
35	Liver	Discolouration, pale.
36	Liver	Discolouration, pale.
37		No findings noted
38		No findings noted
39		No findings noted
40	Liver	Discolouration, pale.

**FEMALES
ALL NECROPSIES**

ANIMAL ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)		
41	No findings noted	Scheduled necropsy, 22Feb2007
42	No findings noted	Scheduled necropsy, 21Feb2007
43	No findings noted	Scheduled necropsy, 19Feb2007
44	No findings noted	Scheduled necropsy, 20Feb2007
45	No findings noted	Scheduled necropsy, 20Feb2007
46	No findings noted	Scheduled necropsy, 19Feb2007
47	No findings noted	Scheduled necropsy, 20Feb2007

APPENDIX 2

**MACROSCOPIC FINDINGS
FEMALES
ALL NECROPSIES**

ANIMAL ORGAN	FINDING	DAY OF DEATH
GROUP 1 (CONTROL)		
48	No findings noted	Scheduled necropsy, 20Feb2007
49	No findings noted	Scheduled necropsy, 21Feb2007
50	No findings noted	Scheduled necropsy, 21Feb2007
GROUP 2 (50 MG/KG)		
51 Uterus	Enlarged. Contains fluid.	Scheduled necropsy, 21Feb2007
52 Cervix	Enlarged.	
53 Adrenal glands	No findings noted Both sides: enlarged.	Scheduled necropsy, 22Feb2007
54	No findings noted	Scheduled necropsy, 19Feb2007
55	No findings noted	Scheduled necropsy, 20Feb2007
56	No findings noted	Scheduled necropsy, 21Feb2007
57	No findings noted	Scheduled necropsy, 22Feb2007
58	No findings noted	Scheduled necropsy, 22Feb2007
59 Skin	Hindleg, right side: alopecia.	Scheduled necropsy, 19Feb2007
60 Stomach	Contents: reddish.	Scheduled necropsy, 20Feb2007
Other, 15Feb2007		
GROUP 3 (150 MG/KG)		
61	No findings noted	Scheduled necropsy, 22Feb2007
62	No findings noted	Scheduled necropsy, 19Feb2007
63	No findings noted	Scheduled necropsy, 21Feb2007
64	No findings noted	Scheduled necropsy, 19Feb2007
65	No findings noted	Scheduled necropsy, 19Feb2007
66 Liver	Right lateral lobe: diaphragmatic Hernia.	Scheduled necropsy, 21Feb2007
67	No findings noted	Scheduled necropsy, 21Feb2007
68	No findings noted	Scheduled necropsy, 21Feb2007
69	No findings noted	Scheduled necropsy, 19Feb2007
70	No findings noted	Scheduled necropsy, 20Feb2007
GROUP 4 (500 MG/KG)		
71	No findings noted	Scheduled necropsy, 21Feb2007
72	No findings noted	Scheduled necropsy, 20Feb2007
73	No findings noted	Scheduled necropsy, 21Feb2007
74 Lungs	Focus/foci, many, gray-white.	Scheduled necropsy, 21Feb2007
75	No findings noted	Scheduled necropsy, 21Feb2007
76	No findings noted	Scheduled necropsy, 21Feb2007
77	No findings noted	Scheduled necropsy, 21Feb2007
78	No findings noted	Scheduled necropsy, 20Feb2007
79	No findings noted	Other, 17Feb2007
80	No findings noted	Scheduled necropsy, 20Feb2007

APPENDIX 2

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
1	451	2.03	1.348	12.08	0.619
2	413	2.02	1.319	10.65	0.324
3	444	—	—	—	—
4	410	1.89	1.149	9.95	0.417
5	421	—	—	—	—
6	437	2.13	1.240	11.73	0.532
7	451	2.14	1.259	12.94	0.445
8	397	—	—	—	—
9	380	—	—	—	—
10	437	—	—	—	—
GROUP 2 (50 MG/KG)					
11	453	—	—	—	—
12	407	2.21	1.273	10.47	0.334
13	410	2.03	1.285	10.75	0.338
14	420	2.13	1.257	10.65	0.369
15	381	—	—	—	—
16	395	2.20	1.405	10.41	0.450
17	410	2.11	1.391	9.82	0.269
18	408	—	—	—	—
19	422	—	—	—	—
20	458	—	—	—	—
GROUP 3 (150 MG/KG)					
21	411	2.25	1.389	11.26	0.405
22	459	2.11	1.490	11.30	0.556
23	375	1.95	1.212	9.74	0.236
24	386	2.11	1.203	9.23	0.311
25	464	2.01	1.447	13.12	0.386
26	400	—	—	—	—
27	455	—	—	—	—
28	425	—	—	—	—
29	396	—	—	—	—
30	388	—	—	—	—
GROUP 4 (500 MG/KG)					
31	412	2.15	1.405	12.49	0.242
32	410	2.11	1.380	11.50	0.347
33	410	—	—	—	—
34	408	2.07	1.453	12.90	0.284
35	381	2.06	1.446	12.98	0.305
36	384	2.08	1.398	12.44	0.248
37	391	—	—	—	—
38	411	—	—	—	—
39	393	—	—	—	—
40	428	—	—	—	—

APPENDIX 2

ORGAN WEIGHTS (GRAM)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1 (CONTROL)					
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1.448
3	—	—	—	4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5	—	—	—	4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.085	1.250	4.01	1.229
8	—	—	—	4.10	1.142
9	—	—	—	3.86	1.344
10	—	—	—	4.25	1.353
GROUP 2 (50 MG/KG)					
11	—	—	—	3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15	—	—	—	3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18	—	—	—	3.72	1.284
19	—	—	—	3.92	1.313
20	—	—	—	3.78	1.199
GROUP 3 (150 MG/KG)					
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26	—	—	—	3.86	1.074
27	—	—	—	3.69	1.157
28	—	—	—	3.79	1.176
29	—	—	—	4.21	1.166
30	—	—	—	3.70	1.158
GROUP 4 (500 MG/KG)					
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33	—	—	—	3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37	—	—	—	3.87	0.886
38	—	—	—	4.57	1.148
39	—	—	—	3.84	1.172
40	—	—	—	4.35	1.124

APPENDIX 2

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
1	451	0.45	0.299	2.68	0.137
2	413	0.49	0.319	2.58	0.078
3	444	---	---	---	---
4	410	0.46	0.280	2.43	0.102
5	421	---	---	---	---
6	437	0.49	0.284	2.68	0.122
7	451	0.47	0.279	2.87	0.099
8	397	---	---	---	---
9	380	---	---	---	---
10	437	---	---	---	---
GROUP 2 (50 MG/KG)					
11	453	---	---	---	---
12	407	0.54	0.313	2.57	0.082
13	410	0.49	0.313	2.62	0.082
14	420	0.51	0.299	2.53	0.088
15	381	---	---	---	---
16	395	0.56	0.356	2.63	0.114
17	410	0.51	0.339	2.39	0.066
18	408	---	---	---	---
19	422	---	---	---	---
20	458	---	---	---	---
GROUP 3 (150 MG/KG)					
21	411	0.55	0.338	2.74	0.099
22	459	0.46	0.325	2.46	0.121
23	375	0.52	0.323	2.80	0.063
24	386	0.55	0.312	2.39	0.081
25	464	0.43	0.312	2.83	0.083
26	400	---	---	---	---
27	455	---	---	---	---
28	425	---	---	---	---
29	396	---	---	---	---
30	388	---	---	---	---
GROUP 4 (500 MG/KG)					
31	412	0.52	0.341	3.03	0.059
32	410	0.51	0.337	2.80	0.085
33	410	---	---	---	---
34	408	0.51	0.356	3.16	0.070
35	381	0.54	0.380	3.41	0.080
36	384	0.54	0.364	3.24	0.065
37	391	---	---	---	---
38	411	---	---	---	---
39	393	---	---	---	---
40	426	---	---	---	---

APPENDIX 2

ORGAN/BODY WEIGHT RATIOS (%)
MALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1 (CONTROL)					
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.285	1.09	0.351
3	---	---	---	0.92	0.308
4	0.69	0.017	0.190	0.93	0.285
5	---	---	---	1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8	---	---	---	1.03	0.288
9	---	---	---	1.02	0.354
10	---	---	---	0.97	0.310
GROUP 2 (50 MG/KG)					
11	---	---	---	0.81	0.298
12	0.79	0.016	0.230	1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15	---	---	---	0.95	0.317
16	0.76	0.015	0.275	0.91	0.327
17	0.86	0.016	0.199	0.73	0.250
18	---	---	---	0.91	0.315
19	---	---	---	0.93	0.311
20	---	---	---	0.83	0.262
GROUP 3 (150 MG/KG)					
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.69	0.016	0.264	0.93	0.268
26	---	---	---	0.97	0.269
27	---	---	---	0.81	0.254
28	---	---	---	0.89	0.277
29	---	---	---	1.06	0.294
30	---	---	---	0.95	0.298
GROUP 4 (500 MG/KG)					
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.020	0.247	0.97	0.222
33	---	---	---	0.97	0.258
34	0.85	0.021	0.224	1.04	0.253
35	0.81	0.020	0.219	0.94	0.268
36	0.75	0.016	0.214	1.00	0.259
37	---	---	---	0.99	0.227
38	---	---	---	1.11	0.279
39	---	---	---	0.98	0.298
40	---	---	---	1.02	0.263

APPENDIX 2

ORGAN WEIGHTS (GRAM)
FEMALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1 (CONTROL)					
42	247	2.00	0.975	9.46	0.183
44	262	1.88	0.902	9.21	0.253
45	271	1.85	0.925	8.99	0.190
47	276	1.93	0.906	8.74	0.298
48	285	1.89	1.043	9.71	0.216
GROUP 2 (50 MG/KG)					
52	280	2.01	1.067	9.94	0.229
53	299	1.94	1.029	10.63	0.203
54	281	1.88	0.904	10.02	0.192
58	269	1.84	1.025	9.85	0.179
59	299	1.88	1.001	10.70	0.327
GROUP 3 (150 MG/KG)					
62	292	1.99	0.981	9.60	0.228
63	271	1.85	0.955	9.31	0.196
64	282	1.85	1.086	11.19	0.185
66	270	1.80	1.046	9.60	0.195
70	302	1.95	0.995	9.54	0.199
GROUP 4 (500 MG/KG)					
71	263	1.86	1.064	9.40	0.177
72	282	1.86	1.037	8.72	0.166
74	291	1.92	1.142	9.58	0.149
78	246	1.80	1.040	8.65	0.116
80	271	1.77	0.961	10.01	0.184

FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)
GROUP 1 (CONTROL)			
42	2.10	0.094	0.941
44	1.95	0.103	0.841
45	1.83	0.100	0.910
47	2.21	0.083	0.869
48	1.97	0.087	0.863
GROUP 2 (50 MG/KG)			
52	2.27	0.110	0.847
53	2.41	0.130	0.978
54	2.01	0.102	0.760
58	2.15	0.091	0.802
59	1.93	0.105	0.995
GROUP 3 (150 MG/KG)			
62	2.40	0.102	0.820
63	2.11	0.111	1.029
64	2.32	0.127	1.122
66	2.21	0.115	0.802
70	2.27	0.113	0.577

APPENDIX 2

ORGAN WEIGHTS (GRAM)
FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)
GROUP 4 (500 MG/KG)			
71	2.38	0.112	0.733
72	2.56	0.109	0.647
74	2.53	0.110	0.870
78	2.20	0.127	0.553
80	2.18	0.106	0.654

APPENDIX 2

ORGAN/BODY WEIGHT RATIOS (%)
FEMALES
END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)
GROUP 1 (CONTROL)					
42	247	0.81	0.395	3.83	0.074
44	262	0.72	0.344	3.52	0.097
45	271	0.68	0.341	3.32	0.070
47	276	0.70	0.328	3.17	0.108
48	285	0.66	0.365	3.41	0.076
GROUP 2 (50 MG/KG)					
52	280	0.72	0.381	3.55	0.082
53	299	0.65	0.344	3.56	0.068
54	281	0.67	0.322	3.57	0.068
58	269	0.68	0.381	3.66	0.067
59	299	0.63	0.335	3.58	0.109
GROUP 3 (150 MG/KG)					
62	292	0.68	0.336	3.29	0.078
63	271	0.68	0.352	3.44	0.072
64	282	0.66	0.385	3.97	0.066
66	270	0.67	0.387	3.56	0.072
70	302	0.65	0.329	3.16	0.066
GROUP 4 (500 MG/KG)					
71	263	0.71	0.405	3.58	0.067
72	282	0.66	0.368	3.09	0.059
74	291	0.66	0.392	3.29	0.051
78	246	0.73	0.423	3.52	0.047
80	271	0.65	0.355	3.69	0.068

FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)
GROUP 1 (CONTROL)			
42	0.85	0.038	0.381
44	0.74	0.039	0.321
45	0.67	0.037	0.336
47	0.80	0.030	0.315
48	0.69	0.031	0.303
GROUP 2 (50 MG/KG)			
52	0.81	0.039	0.303
53	0.80	0.043	0.327
54	0.71	0.036	0.270
58	0.80	0.034	0.298
59	0.64	0.035	0.333
GROUP 3 (150 MG/KG)			
62	0.82	0.035	0.281
63	0.78	0.041	0.380
64	0.82	0.045	0.398
66	0.82	0.043	0.297
70	0.75	0.037	0.191

APPENDIX 2

ORGAN/BODY WEIGHT RATIOS (%)
FEMALES
END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)
GROUP 4 (500 MG/KG)			
71	0.90	0.043	0.279
72	0.91	0.039	0.229
74	0.87	0.038	0.299
78	0.89	0.052	0.225
80	0.80	0.039	0.241

APPENDIX 2

**BREEDING DATA PER LITTER
F0-GENERATION - LACTATION**

LITTER	GESTATION	— FIRST LITTER CHECK —						P.NATAL LOSS			LIVING PUPS		
		DURATION OF DEAD PUPS			LIVING PUPS			DAYS 0 - 4		CULLED	DAY 4 P.P.		
		M	F	M	F	TOT.	M	F	PUPS TOT.	M	F	TOT.	
GROUP 1 (CONTROL)													
41	22	0	0	12	6	18	0	0	0	12	6	18	
42	21	1	0	10	9	19	0	0	0	10	9	19	
43	21	1	0	3	11	14	0	0	0	3	11	14	
44	21	0	0	6	10	16	0	0	0	6	10	16	
45	20	0	0	9	6	15	0	0	0	9	6	15	
46	22	0	0	8	6	14	0	0	0	8	6	14	
47	22	0	0	5	10	15	0	0	0	5	10	15	
48	20	0	0	6	10	16	0	0	0	6	10	16	
49	22	0	0	6	11	17	0	0	0	6	11	17	
TOTAL		2	0	65	79	144	0	0	0	65	79	144	
N		9	9	9	9	9	9	9	9	9	9	9	
MEAN		21.2	0.2	0.0	7.2	8.8	16.0	0.0	0.0	0.0	7.2	8.8	16.0
ST.DEV.		0.8	0.4	0.0	2.8	2.2	1.7	0.0	0.0	0.0	2.8	2.2	1.7

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	GESTATION	-- FIRST LITTER CHECK --						P.NATAL LOSS			LIVING PUPS			
		DURATION OF GESTATION			DEAD PUPS	LIVING PUPS	TOT.	DAYS 0 - 4	CULLED	PUPS TOT.	DAY 4 P.P.	M	F	TOT.
GROUP 2 (50 MG/KG)														
52	22	0	0	8	8	16	0	0	0	8	7	15		
53	21	1	0	12	6	18	0	0	0	12	6	18		
54	21	0	0	11	7	18	0	0	0	11	7	18		
56	22	0	0	4	3	7	0	0	0	4	3	7		
57	22	0	0	2	13	15	0	1	0	2	12	14		
58	21	0	0	7	10	17	0	0	0	7	10	17		
59	21	0	0	6	10	16	0	0	0	6	10	16		
60	22	0	0	1	12	13	1	12	0	0	0	0		
TOTAL		1	0	51	69	120	1	13	0	50	55	105		
N	8	8	8	8	8	8	8	8	8	8	8	8		
MEAN	21.5	0.1	0.0	6.4	8.6	15.0	0.1	1.6	0.0	6.3	6.9	13.1		
ST.DEV.	0.5	0.4	0.0	4.0	3.3	3.6	0.4	4.2	0.0	4.2	3.9	6.4		

APPENDIX 2

**BREEDING DATA PER LITTER
F0-GENERATION - LACTATION**

LITTER	GESTATION	— FIRST LITTER CHECK —						P.NATAL LOSS			LIVING PUPS				
		DURATION OF GESTATION			DEAD PUPS			LIVING PUPS			DAYS 0 - 4		CULLED	DAY 4	P.P.
		M	F	M	F	TOT.	M	F	PUPS TOT.	M	F	TOT.			
GROUP 3 (150 MG/KG)															
61	22	0	0	8	9	17	0	0	0	8	9	17			
62	21	0	0	8	6	14	0	0	0	8	6	14			
63	22	0	0	11	9	20	0	2	0	11	7	18			
64	21	0	0	4	14	18	0	0	0	4	14	18			
65	21	0	0	6	7	13	0	0	0	6	7	13			
66	20	0	0	8	8	16	0	0	0	8	8	16			
67	21	0	0	7	10	17	0	0	0	7	9	16			
68	22	0	0	11	6	17	3	1	0	8	5	13			
69	21	0	0	7	11	18	2	0	0	5	11	16			
70	21	2	1	11	6	17	0	0	0	11	6	17			
TOTAL		2	1	81	86	167	5	3	0	76	82	158			
N	10	10	10	10	10	10	10	10	10	10	10	10			
MEAN	21.2	0.2	0.1	8.1	8.6	16.7	0.5	0.3	0.0	7.6	8.2	15.8			
ST.DEV.	0.6	0.6	0.3	2.3	2.6	2.0	1.1	0.7	0.0	2.3	2.7	1.9			

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	DURATION OF GESTATION	-- FIRST LITTER CHECK --						P.NATAL LOSS			LIVING PUPS			
		DEAD PUPS	LIVING PUPS	M	F	M	F	TOT.	DAYS 0 - 4	CULLED	DAY 4 P.P.	M	F	TOT.
GROUP 4 (500 MG/KG)														
71	22	0	0	2	2	4	0	0	0		2	2	4	
72	22	0	0	5	2	7	0	0	0		5	2	7	
74	22	0	0	5	4	9	0	0	0		5	4	9	
76	22	0	0	2	6	8	0	0	0		2	6	8	
78	22	0	0	6	5	11	4	4	0		2	1	3	
79	21	3	0	0	2	2	0	0	0		0	0	0	
80	22	0	0	3	4	7	0	0	0		3	4	7	
TOTAL		3	0	23	25	48	4	4	0		19	19	38	
N		7	7	7	7	7	7	7	7		7	7	7	
MEAN		21.9	0.4	0.0	3.3	3.6	6.9	0.6	0.6	0.0		2.7	2.7	5.4
ST.DEV.		0.4	1.1	0.0	2.1	1.6	3.0	1.5	1.5	0.0		1.8	2.1	3.2

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	BREEDING LOSS		LIVING PUPS		
	DAYS 5 - 21		DAY 21 P.P.		
	M	F	M	F	TOT.
GROUP 1 (CONTROL)					
41	0	0	0	0	0
42	0	0	0	0	0
43	0	0	0	0	0
44	0	0	0	0	0
45	0	0	0	0	0
46	0	0	0	0	0
47	0	0	0	0	0
48	0	0	0	0	0
49	0	0	0	0	0
TOTAL	0	0	0	0	0
N	9	9	9	9	9
MEAN	0.0	0.0	0.0	0.0	0.0
ST.DEV.	0.0	0.0	0.0	0.0	0.0

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	BREEDING LOSS DAYS 5 - 21		LIVING PUPS DAY 21 P.P.		
	M	F	M	F	TOT.
GROUP 2 (50 MG/KG)					
52	0	0	0	0	0
53	0	0	0	0	0
54	0	0	0	0	0
56	0	0	0	0	0
57	0	0	0	0	0
58	0	0	0	0	0
59	0	0	0	0	0
60	0	0	0	0	0
TOTAL	0	0	0	0	0
N	8	8	8	8	8
MEAN	0.0	0.0	0.0	0.0	0.0
ST.DEV.	0.0	0.0	0.0	0.0	0.0

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	BREEDING LOSS		LIVING PUPS		
	DAYS 5 - 21		DAY 21 P.P.		
	M	F	M	F	TOT.
GROUP 3 (150 MG/KG)					
61	0	0	0	0	0
62	1	0	0	0	0
63	0	0	0	0	0
64	0	0	0	0	0
65	0	0	0	0	0
66	0	0	0	0	0
67	0	0	0	0	0
68	0	0	0	0	0
69	0	0	0	0	0
70	0	0	0	0	0
TOTAL	1	0	0	0	0
N	10	10	10	10	10
MEAN	0.1	0.0	0.0	0.0	0.0
ST.DEV.	0.3	0.0	0.0	0.0	0.0

APPENDIX 2

BREEDING DATA PER LITTER
F0-GENERATION - LACTATION

LITTER	BREEDING LOSS		LIVING PUPS		
	DAYS 5 - 21		DAY 21 P.P.		
	M	F	M	F	TOT.
GROUP 4 (500 MG/KG)					
71	0	0	0	0	0
72	0	0	0	0	0
74	0	0	0	0	0
76	0	0	0	0	0
78	0	0	0	0	0
79	0	0	0	0	0
80	0	0	0	0	0
TOTAL	0	0	0	0	0
N	7	7	7	7	7
MEAN	0.0	0.0	0.0	0.0	0.0
ST.DEV.	0.0	0.0	0.0	0.0	0.0

APPENDIX 2

**MEAN BODY WEIGHTS OF PUPS PER LITTER (GRAM)
F0-GENERATION - LACTATION**

LITTER	SEX	DAY 1	DAY 4
GROUP 1 (CONTROL)			
41	M	6.4	9.3
	F	5.9	7.8
	M+F	6.2	8.8
42	M	5.9	8.4
	F	5.7	7.7
	M+F	5.8	8.1
43	M	6.6	9.7
	F	6.4	9.5
	M+F	6.4	9.6
44	M	6.0	8.5
	F	5.5	7.7
	M+F	5.7	8.0
45	M	6.6	8.9
	F	6.0	8.4
	M+F	6.3	8.7
46	M	7.3	11.5
	F	7.3	11.2
	M+F	7.3	11.4
47	M	7.4	10.8
	F	6.9	10.4
	M+F	7.1	10.6
48	M	6.4	8.8
	F	5.9	8.1
	M+F	6.1	8.3
49	M	6.6	9.8
	F	6.3	9.2
	M+F	6.4	9.4
GROUP 2 (50 MG/KG)			
52	M	6.6	10.2
	F	6.4	9.6
	M+F	6.5	9.9
53	M	6.5	9.4
	F	6.1	8.5
	M+F	6.4	9.1
54	M	6.3	8.8
	F	5.8	7.7
	M+F	6.1	8.4
56	M	7.8	13.0
	F	7.8	13.0
	M+F	7.8	13.0
57	M	6.3	10.3
	F	6.1	9.8
	M+F	6.2	9.8
58	M	6.4	9.1
	F	6.0	8.6
	M+F	6.2	8.8
59	M	6.7	10.2
	F	6.3	9.6
	M+F	6.5	9.8
60	M	7.4	--
	F	7.3	--
	M+F	7.3	--

APPENDIX 2

**MEAN BODY WEIGHTS OF PUPS PER LITTER (GRAM)
F0-GENERATION - LACTATION**

LITTER	SEX	DAY 1	DAY 4
GROUP 3 (150 MG/KG)			
61	M	6.7	9.1
	F	5.8	7.7
	M+F	6.2	8.3
62	M	6.4	9.1
	F	6.0	8.4
	M+F	6.2	8.8
63	M	6.3	9.2
	F	5.8	8.4
	M+F	6.1	8.9
64	M	6.3	9.1
	F	6.0	8.2
	M+F	6.0	8.4
65	M	6.1	9.6
	F	6.1	9.5
	M+F	6.1	9.6
66	M	6.4	8.4
	F	5.8	7.4
	M+F	6.1	7.9
67	M	6.3	9.1
	F	5.9	8.4
	M+F	6.1	8.7
68	M	6.9	10.9
	F	6.2	9.8
	M+F	6.7	10.5
69	M	5.9	8.4
	F	5.3	7.7
	M+F	5.6	7.9
70	M	6.1	8.1
	F	5.7	7.5
	M+F	5.9	7.9
GROUP 4 (500 MG/KG)			
71	M	7.6	11.1
	F	6.6	9.9
	M+F	7.1	10.5
72	M	6.2	9.2
	F	6.8	10.3
	M+F	6.3	9.5
74	M	6.3	9.5
	F	6.7	10.2
	M+F	6.5	9.8
76	M	7.6	11.2
	F	6.6	9.8
	M+F	6.8	10.2
78	M	5.6	8.0
	F	5.4	7.3
	M+F	5.5	7.8
79	M	5.7	--
	F	5.3	--
	M+F	5.5	--
80	M	7.0	10.8
	F	6.7	10.3
	M+F	6.8	10.5

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 1 (CONTROL)

41	1	M	6.8	10.3
	2	M	5.6	8.2
	3	M	5.9	8.8
	4	M	6.7	9.2
	5	M	7.0	10.0
	6	M	6.4	10.1
	7	M	6.6	9.8
	8	M	6.1	8.6
	9	M	6.4	8.7
	10	M	6.1	9.2
	11	M	6.5	9.4
	12	M	6.2	9.1
	13	F	6.1	8.5
	14	F	5.5	7.3
	15	F	5.6	7.6
	16	F	6.4	9.5
	17	F	5.2	5.8
	18	F	6.4	8.2
42	1	M	5.8	8.8
	2	M	6.0	8.7
	3	M	6.1	8.9
	4	M	6.1	8.7
	5	M	6.3	9.1
	6	M	5.1	6.5
	7	M	5.6	8.5
	8	M	5.5	8.2
	9	M	6.7	8.9
	10	M	—	—
	11	F	5.7	7.9
	12	F	5.8	7.9
	13	F	5.5	7.4
	14	M	6.2	8.2
	15	F	5.5	7.3
	16	F	5.8	8.0
	17	F	5.2	7.7
	18	F	5.2	6.9
	19	F	6.0	8.5
	20	F	6.2	7.9
43	1	M	6.4	10.0
	2	M	6.7	9.0
	3	M	6.5	9.9
	4	M	—	—
	5	F	6.3	9.4
	6	F	6.8	10.0
	7	F	6.4	9.5
	8	F	6.4	10.2
	9	F	6.6	10.2
	10	F	5.9	9.1
	11	F	6.1	8.7
	12	F	6.6	9.6
	13	F	6.3	9.9
	14	F	6.0	8.8
	15	F	6.6	9.4
44	1	M	5.7	8.3
	2	M	6.5	9.7
	3	M	5.7	7.4
	4	M	6.1	8.6
	5	M	5.7	8.1
	6	M	6.3	8.9
	7	F	6.0	8.5
	8	F	5.9	8.8
	9	F	5.4	7.4
	10	F	5.4	8.3

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION – LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 1 (CONTROL)

	11	F	5.2	6.9
	12	F	5.9	8.6
	13	F	5.0	6.2
	14	F	5.0	6.9
	15	F	5.7	8.1
	16	F	5.1	7.0
45	1	M	5.9	7.8
	2	M	6.9	9.6
	3	M	6.6	8.1
	4	M	6.9	9.3
	5	M	6.8	8.8
	6	M	6.9	9.7
	7	M	6.3	8.7
	8	M	6.3	9.0
	9	M	6.5	9.4
	10	F	6.0	9.1
	11	F	6.0	8.7
	12	F	6.5	9.1
	13	F	5.5	7.6
	14	F	5.7	7.8
	15	F	6.2	8.3
46	1	M	7.9	12.4
	2	M	7.0	11.6
	3	M	7.2	10.8
	4	M	6.9	11.2
	5	M	7.0	10.8
	6	M	7.6	11.9
	7	M	7.1	11.2
	8	M	7.3	11.9
	9	F	7.3	11.0
	10	F	7.3	11.3
	11	F	7.2	11.3
	12	F	7.1	10.5
	13	F	7.4	11.7
	14	F	7.6	11.4
47	1	M	7.5	11.4
	2	M	7.1	10.0
	3	M	7.3	10.3
	4	M	7.1	10.8
	5	M	8.0	11.7
	6	F	7.1	11.3
	7	F	6.5	10.1
	8	F	7.0	10.7
	9	F	6.9	10.9
	10	F	7.2	10.3
	11	F	6.7	10.5
	12	F	6.5	10.1
	13	F	7.4	10.6
	14	F	6.6	9.6
	15	F	7.0	10.3
48	1	M	7.0	9.9
	2	M	6.7	9.2
	3	M	6.1	8.4
	4	M	5.8	7.8
	5	F	6.5	8.7
	6	F	5.4	7.5
	7	M	6.9	9.6
	8	M	6.0	7.9
	9	F	6.0	8.8
	10	F	6.0	8.1
	11	F	6.2	8.3
	12	F	6.4	9.0
	13	F	6.4	8.8

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 1 (CONTROL)

	14	F	4.8	5.8
	15	F	5.6	7.4
	16	F	5.9	8.3
49	1	M	7.0	11.2
	2	M	5.8	8.2
	3	M	7.2	10.0
	4	M	7.4	11.3
	5	M	6.0	9.3
	6	M	6.2	9.0
	7	F	6.4	9.9
	8	F	5.8	8.3
	9	F	5.6	8.3
	10	F	6.6	9.8
	11	F	5.8	8.5
	12	F	6.2	9.5
	13	F	6.7	9.3
	14	F	6.2	8.3
	15	F	6.7	8.5
	16	F	6.8	10.3
	17	F	6.7	10.3

GROUP 2 (50 MG/KG)

52	1	M	6.8	11.6
	2	M	6.4	9.5
	3	M	6.1	9.3
	4	M	6.7	11.1
	5	M	6.8	10.2
	6	M	6.5	9.8
	7	M	6.7	9.8
	8	M	6.6	10.2
	9	F	6.6	8.5
	10	F	6.0	9.9
	11	F	6.1	9.6
	12	F	6.2	9.3
	13	F	6.6	—
	14	F	6.4	9.5
	15	F	6.7	10.1
	16	F	6.3	10.2
53	1	M	6.3	9.2
	2	M	6.8	9.8
	3	M	6.8	9.2
	4	M	6.1	9.2
	5	M	6.4	9.1
	6	M	6.5	9.6
	7	M	6.6	9.5
	8	M	7.1	9.9
	9	M	6.5	9.3
	10	M	6.1	9.0
	11	M	6.3	8.9
	12	M	6.5	9.6
	13	M	—	—
	14	F	6.1	8.6
	15	F	5.8	8.2
	16	F	6.1	8.3
	17	F	6.4	9.2
	18	F	5.9	8.2
	19	F	6.1	8.2

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 2 (50 MG/KG)

54	1	M	6.4	8.9
	2	M	6.5	9.2
	3	M	6.1	8.6
	4	M	6.0	8.1
	5	M	6.5	9.3
	6	M	6.3	8.4
	7	M	6.1	8.5
	8	M	6.6	10.1
	9	M	6.4	9.2
	10	M	6.1	8.8
	11	F	6.2	8.3
	12	F	6.0	8.9
	13	F	5.7	7.7
	14	M	5.9	8.0
	15	F	5.5	7.1
	16	F	5.8	6.8
	17	F	5.8	7.5
	18	F	5.6	8.0
56	1	M	8.1	13.5
	2	M	7.6	12.2
	3	M	7.6	13.3
	4	M	7.9	13.2
	5	F	7.7	13.1
	6	F	7.9	13.3
	7	F	7.7	12.5
57	1	M	6.8	10.9
	2	M	5.8	9.8
	3	F	5.9	9.6
	4	F	5.8	8.4
	5	F	6.5	10.3
	6	F	5.8	9.4
	7	F	6.2	9.8
	8	F	6.7	9.9
	9	F	5.5	--
	10	F	6.8	11.5
	11	F	5.1	7.5
	12	F	6.3	10.0
	13	F	5.9	9.2
	14	F	7.0	11.6
	15	F	6.3	9.9
58	1	M	6.1	9.2
	2	F	5.9	8.4
	3	M	6.6	9.5
	4	M	6.2	7.8
	5	M	6.5	9.3
	6	M	6.0	8.9
	7	M	6.6	9.6
	8	M	6.5	9.5
	9	F	5.8	8.8
	10	F	6.0	9.1
	11	F	6.5	9.2
	12	F	6.2	8.8
	13	F	6.3	9.6
	14	F	5.8	7.2
	15	F	6.3	8.9
	16	F	5.9	8.3
	17	F	5.8	7.9

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 2 (50 MG/KG)

59	1	M	6.2	9.8
	2	M	7.1	11.4
	3	M	6.3	8.9
	4	M	6.7	10.5
	5	F	6.0	8.9
	6	M	6.7	10.0
	7	M	7.2	10.9
	8	F	6.2	9.0
	9	F	6.0	9.4
	10	F	6.6	10.1
	11	F	5.9	9.2
	12	F	6.8	9.9
	13	F	7.0	10.7
	14	F	6.5	9.8
	15	F	6.0	9.7
	16	F	6.2	9.4

60

	1	M	7.4	
	2	F	7.6	
	3	F	6.8	
	4	F	7.7	
	5	F	7.8	
	6	F	7.4	
	7	F	7.2	
	8	F	6.8	
	9	F	7.5	
	10	F	6.9	
	11	F	7.7	
	12	F	7.0	
	13	F	7.5	

GROUP 3 (150 MG/KG)

61	1	M	6.7	8.9
	2	M	6.4	8.8
	3	M	6.8	9.5
	4	M	7.1	9.2
	5	M	6.6	8.6
	6	M	6.6	9.2
	7	M	6.7	9.5
	8	M	6.5	8.8
	9	F	5.9	8.1
	10	F	6.2	7.9
	11	F	6.4	8.7
	12	F	5.6	7.7
	13	F	5.7	7.7
	14	F	5.8	8.0
	15	F	5.7	7.4
	16	F	5.4	6.7
	17	F	5.3	6.7

62

	1	M	5.8	8.5
	2	M	6.7	8.5
	3	M	6.4	9.4
	4	M	6.4	9.1
	5	M	6.2	8.9
	6	M	6.1	9.4
	7	M	6.7	9.3
	8	M	6.7	9.6
	9	F	5.9	8.9
	10	F	5.9	8.9
	11	F	6.2	9.4
	12	F	5.9	8.0
	13	F	6.0	7.9
	14	F	6.0	7.2

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 3 (150 MG/KG)

63	1	M	7.2	10.2
	2	M	6.2	9.0
	3	M	6.3	9.0
	4	M	5.5	8.4
	5	M	6.5	9.8
	6	M	6.3	8.5
	7	M	6.0	8.3
	8	M	6.6	10.6
	9	M	6.2	9.3
	10	M	6.1	8.9
	11	F	5.9	8.3
	12	F	5.6	8.5
	13	F	5.8	--
	14	F	6.0	--
	15	F	6.1	7.8
	16	F	5.9	8.1
	17	M	6.8	9.5
	18	F	5.6	8.5
	19	F	5.8	9.1
	20	F	5.8	8.3
64	1	M	6.0	9.0
	2	M	6.2	8.8
	3	M	6.7	9.6
	4	M	6.2	8.8
	5	F	6.5	9.3
	6	F	5.8	8.2
	7	F	5.7	7.5
	8	F	6.3	8.8
	9	F	6.1	8.8
	10	F	6.0	8.4
	11	F	6.1	8.7
	12	F	5.9	7.9
	13	F	6.3	8.8
	14	F	5.9	7.5
	15	F	5.7	8.3
	16	F	5.8	8.0
	17	F	6.0	8.2
	18	F	5.6	7.1
65	1	M	6.2	10.1
	2	M	5.5	8.1
	3	M	6.4	10.3
	4	M	6.3	9.7
	5	M	6.6	10.2
	6	M	5.7	9.3
	7	F	6.3	9.8
	8	F	6.2	10.2
	9	F	6.0	9.6
	10	F	6.0	9.3
	11	F	6.1	9.2
	12	F	6.1	9.3
	13	F	6.1	9.2
66	1	M	6.4	8.6
	2	M	6.5	8.0
	3	M	6.3	8.6
	4	M	6.5	7.9
	5	M	6.7	9.2
	6	M	6.7	8.9
	7	M	5.7	8.0
	8	M	6.3	8.5
	9	F	6.0	7.9
	10	F	5.8	7.8
	11	F	6.1	7.9
	12	F	6.3	8.1

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 3 (150 MG/KG)

	13	F	5.0	6.1
	14	F	6.0	6.9
	15	F	5.6	7.2
	16	F	5.7	7.5
67	1	M	5.8	9.0
	2	M	6.2	9.3
	3	M	6.2	8.3
	4	M	6.2	8.6
	5	M	6.5	9.2
	6	M	6.6	10.1
	7	M	6.6	9.5
	8	F	5.8	8.4
	9	F	6.1	8.5
	10	F	6.6	10.0
	11	F	6.3	9.4
	12	F	6.4	8.7
	13	F	5.7	7.9
	14	F	5.1	—
	15	F	5.6	8.2
	16	F	5.8	7.4
	17	F	5.5	7.6
68	1	M	6.5	10.6
	2	M	5.8	—
	3	M	7.2	—
	4	M	7.1	11.1
	5	M	7.2	11.7
	6	M	7.1	9.6
	7	M	6.0	—
	8	M	7.6	12.3
	9	M	7.0	11.7
	10	M	7.1	10.0
	11	M	7.2	10.7
	12	F	6.9	11.0
	13	F	7.0	10.7
	14	F	6.5	9.4
	15	F	6.3	9.8
	16	F	5.2	8.1
	17	F	5.4	—
69	1	M	5.1	7.4
	2	M	5.8	7.8
	3	M	6.2	8.6
	4	M	6.3	9.2
	5	M	5.5	—
	6	M	6.0	—
	7	M	6.4	9.3
	8	F	5.3	7.8
	9	F	5.3	8.7
	10	F	5.2	7.7
	11	F	4.6	5.8
	12	F	6.2	9.8
	13	F	5.8	8.3
	14	F	5.4	7.9
	15	F	5.3	6.6
	16	F	5.3	7.7
	17	F	4.8	7.0
	18	F	5.5	7.0
70	1	M	6.6	8.7
	2	M	6.4	8.9
	3	M	5.9	7.9
	4	M	5.9	7.9
	5	M	6.0	8.2
	6	M	6.0	7.9
	7	M	6.0	8.6

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 3 (150 MG/KG)

8	M	5.9	7.1
9	M	6.0	8.7
10	M	--	--
11	M	--	--
12	F	6.0	8.3
13	F	5.8	7.6
14	M	6.3	8.0
15	F	5.5	7.0
16	F	5.7	8.2
17	M	5.7	7.2
18	F	5.4	6.8
19	F	5.6	7.3
20	F	--	--

GROUP 4 (500 MG/KG)

71	1	M	7.9	12.0
	2	M	7.3	10.2
	3	F	6.5	9.7
	4	F	6.7	10.2
72	1	M	6.7	10.3
	2	M	5.0	7.9
	3	M	6.3	9.0
	4	M	6.4	9.5
	5	M	6.4	9.6
	6	F	6.6	10.2
	7	F	7.0	10.4
74	1	M	6.0	9.7
	2	M	5.4	7.8
	3	M	6.8	10.1
	4	M	6.9	11.2
	5	M	6.3	8.7
	6	F	6.5	9.3
	7	F	7.1	10.8
	8	F	6.9	10.7
	9	F	6.4	10.1
76	1	M	7.8	11.5
	2	M	7.4	10.9
	3	F	7.1	10.8
	4	F	7.1	10.4
	5	F	7.2	10.6
	6	F	7.0	10.0
	7	F	6.1	9.3
	8	F	5.1	7.8
78	1	M	5.7	8.5
	2	M	5.3	7.5
	3	M	5.5	--
	4	M	5.9	--
	5	M	5.8	--
	6	M	5.8	--
	7	F	5.6	7.3
	8	F	5.4	--
	9	F	5.4	--
	10	F	5.4	--
	11	F	5.3	--
79	1	M	6.1	
	2	M	5.2	
	3	M	--	
	4	F	5.4	
	5	F	5.3	

APPENDIX 2

**BODY WEIGHTS OF PUPS (GRAM)
F0-GENERATION - LACTATION**

LITTER PUP SEX DAY 1 DAY 4

GROUP 4 (500 MG/KG)

80	1	M	6.9	10.8
	2	M	7.9	12.7
	3	M	6.1	8.8
	4	F	5.7	8.0
	5	F	6.6	9.8
	6	F	7.3	11.7
	7	F	7.3	11.6

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 1 (CONTROL)			
LITTER 41	1 M	DAY 5 Planned Necropsy 17FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 F	DAY 5 Planned Necropsy	FLC No findings DAY 4 Small LLC Small MACRO No findings
	18 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 42	1 M	DAY 5 Planned Necropsy 16FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

INDIVIDUAL PUP DATA F0-GENERATION - LACTATION

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 1 (CONTROL)			
3	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
4	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
5	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
6	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO Small, no milk
7	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
8	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
9	M	DAY 5 Planned Necropsy	FLC No findings DAY 4 Red spot neck LLC No findings MACRO No milk
10	M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO Cannibalism, no milk
11	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
12	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
13	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
14	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
15	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
16	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
17	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
18	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
19	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
20	F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 43	1	M DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
14FEB2007			
2	M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

**FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS**

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 1 (CONTROL)			
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
	5 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F	DAY 5 Planned Necropsy	FLC Read spot head LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC Read spot back LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 44 1 M DAY 5 Planned Necropsy 15FEB2007			
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 1 (CONTROL)			
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
	10 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC Small LLC No findings MACRO No milk
LITTER 45 15FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 1 (CONTROL)			
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 46	1 M	DAY 5 Planned Necropsy 14FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC Red spot back LLC No findings MACRO No milk
LITTER 47	1 M	DAY 5 Planned Necropsy 15FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 1 (CONTROL)			
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC Red spot head LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 48 1 M DAY 6 Planned Necropsy 14FEB2007			
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 6 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	5 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 F	DAY 6 Planned Necropsy	FLC Smaal LLC No findings MACRO Small
	7 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 1 (CONTROL)			
	8 M	DAY 6 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	9 F	DAY 6 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO Small
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 F	DAY 6 Planned Necropsy	FLC Small DAY 4 Small LLC No findings MACRO Small
	15 F	DAY 6 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	16 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 49	1 M	DAY 5 Planned Necropsy 16FEB2007	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 1 (CONTROL)			
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
GROUP 2 (50 MG/KG)			
LITTER 52	1 M	DAY 5 Planned Necropsy 17FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 4 Found death	FLC No findings LLC No findings MACRO No milk

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 2 (50 MG/KG)			
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 53	1 M	DAY 6 Planned Necropsy 13FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 6 Planned Necropsy	FLC Red spot back LLC No findings MACRO No milk
	9 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
	14 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 2 (50 MG/KG)			
	18 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	19 F	DAY 6 Planned Necropsy	FLC Red spots back LLC No findings MACRO No milk
LITTER 54 15FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	17 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	18 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 2 (50 MG/KG)			
LITTER 56	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
17FEB2007	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 57	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
17FEB2007	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 2 Missing	FLC No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 2 (50 MG/KG)			
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 58 1 M DAY 6 Planned Necropsy 13FEB2007			
	2 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 F	DAY 6 Planned Necropsy	FLC Red spot back LLC No findings MACRO No milk
LITTER 69 1 M DAY 5 Planned Necropsy 15FEB2007			
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 2 (50 MG/KG)			
	3 M DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F DAY 5	Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 60	1 M DAY 1	Killed in extremis 14FEB2007	FLC No findings LLC No findings MACRO Canibalism
	2 F DAY 1	Killed in extremis	FLC No findings LLC No findings MACRO Missing
	3 F DAY 1	Killed in extremis	FLC No findings LLC No findings MACRO No findings
	4 F DAY 1	Killed in extremis	FLC No findings LLC No findings MACRO Canibalism
	5 F DAY 1	Killed in extremis	FLC No findings LLC No findings MACRO Canibalism
	6 F DAY 1	Killed in extremis	FLC No findings LLC No findings MACRO Canabalism, stomach not present

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 2 (50 MG/KG)			
	7 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism
	8 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism
	9 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism
	10 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism
	11 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism
	12 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Canabalism, stomach not present
	13 F	DAY 1 Killed in extremis	FLC No findings LLC No findings MACRO Missing
GROUP 3 (150 MG/KG)			
LITTER 61	1 M	DAY 5 Planned Necropsy 17FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	17 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 62 1 M DAY 6 Planned Necropsy 13FEB2007			
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 6 Missing	FLC No findings
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 6 Planned Necropsy	FLC Pale LLC No findings MACRO No findings
	14 F	DAY 6 Planned Necropsy	FLC Pale LLC No findings MACRO No findings
LITTER 63 1 M DAY 5 Planned Necropsy 16FEB2007			
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 3 Missing	FLC No findings LLC No findings
	14 F	DAY 3 Missing	FLC No findings LLC No findings
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	18 F	DAY 5 Planned Necropsy	FLC Red spot neck LLC No findings MACRO No milk
	19 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	20 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 64	1 M	DAY 6 Planned Necropsy 13FEB2007	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER	PUP	END OF P.P. PHASE	FINDINGS
DELIVERY			
GROUP 3 (150 MG/KG)			
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	15 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	17 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	18 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 65			
13FEB2007			
	1 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	6 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 66	1 M	DAY 5 Planned Necropsy 16FEB2007	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 67	1 M	DAY 5 Planned Necropsy 16FEB2007	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 3 Found death	FLC Blue nose DAY 2 Blue nose LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	17 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
LITTER 68 1 M DAY 5 Planned Necropsy 16FEB2007			
	2 M	DAY 3 Missing	FLC No findings
	3 M	DAY 3 Missing	FLC No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings DAY 3 Wound nose DAY 4 Scab nose DAY 5 Red nose LLC Red nose MACRO No milk
	7 M	DAY 4 Missing	FLC No findings
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	11 M	DAY 5 Planned Necropsy	FLC Wound left hindleg DAY 2 Scab left hindleg DAY 3 Scab left hindleg DAY 4 Scab left hindleg DAY 5 Scab left hindleg LLC Scab left hindleg MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC No findings DAY 4 Blue belly DAY 5 Blue belly LLC Blue belly MACRO No milk
LITTER 69 1 M DAY 6 Planned Necropsy 13FEB2007			
	17 F	DAY 3 Missing	FLC No findings
	2 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	3 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 4 Spontaneous death	FLC Red spot nose LLC No findings MACRO No milk
	6 M	DAY 4 Missing	FLC No findings
	7 M	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	9 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	10 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	11 F	DAY 6 Planned Necropsy	FLC Small DAY 4 Small DAY 5 Small DAY 6 Small LLC Small MACRO No findings
	12 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	13 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	14 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	15 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	16 F	DAY 6 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	17 F	DAY 6 Planned Necropsy	FLC Small LLC No findings MACRO No findings
	18 F	DAY 6 Planned Necropsy	FLC Swelling head LLC No findings MACRO No findings
LITTER 70 15FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION – LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 3 (150 MG/KG)			
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	10 M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
	11 M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
	12 F	DAY 5 Planned Necropsy	FLC No findings DAY 2 Red nose DAY 3 Red nose, red spots tail DAY 4 Red tail apex LLC Red tail apex MACRO No milk
	13 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	14 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	15 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	16 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	17 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	18 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	19 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	20 F	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
GROUP 4 (500 MG/KG)			
LITTER 71	1 M	DAY 5 Planned Necropsy 16FEB2007	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk

FLC – FIRST LITTER CHECK, DAY P.P. – CLINICAL SIGNS,
LLC – LAST LITTER CHECK, MACRO – MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 4 (500 MG/KG)			
	3 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 72 1 M DAY 5 Planned Necropsy 15FEB2007			
	2 M	DAY 5 Planned Necropsy	FLC Red spot back LLC No findings MACRO No findings FLC Small DAY 2 Small DAY 3 Small DAY 4 Small LLC Small MACRO Small, no milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 74 1 M DAY 5 Planned Necropsy 16FEB2007			
	2 M	DAY 5 Planned Necropsy	FLC No findings DAY 2 Blue belly, no milk DAY 3 Blue belly LLC No findings MACRO No milk
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	9 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS ,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 4 (500 MG/KG)			
LITTER 76 16FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	3 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	4 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	5 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No milk
	8 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
LITTER 78 15FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 2 Missing	FLC No findings
	4 M	DAY 2 Missing	FLC No findings
	5 M	DAY 2 Missing	FLC No findings
	6 M	DAY 2 Missing	FLC Weak, blue
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	8 F	DAY 2 Missing	FLC No findings
	9 F	DAY 2 Missing	FLC No findings
	10 F	DAY 2 Missing	FLC No findings
	11 F	DAY 2 Missing	FLC Weak, blue
LITTER 79 15FEB2007	1 M	DAY 1 Dead at FLC	FLC No findings LLC No findings MACRO No milk
	2 M	DAY 1 Dead at FLC	FLC No findings LLC No findings MACRO No milk
	3 M	DAY 1 Dead at FLC	FLC Dead LLC No findings MACRO No milk
	4 F	DAY 2 Found death	FLC No findings LLC No findings MACRO No milk
	5 F	DAY 2 Found death	FLC No findings LLC No findings MACRO No milk
LITTER 80 15FEB2007	1 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

APPENDIX 2

**INDIVIDUAL PUP DATA
F0-GENERATION - LACTATION**

LITTER DELIVERY	PUP	END OF P.P. PHASE	FINDINGS
GROUP 4 (500 MG/KG)			
	2 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	3 M	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	4 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	5 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	6 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings
	7 F	DAY 5 Planned Necropsy	FLC No findings LLC No findings MACRO No findings

FLC - FIRST LITTER CHECK, DAY P.P. - CLINICAL SIGNS,
LLC - LAST LITTER CHECK, MACRO - MACROSCOPIC FINDINGS

FOR PUBLIC DISCLOSURE

Support Information for Confidentiality Claims

- 1. Is your company asserting this confidential business information (CBI) claim on its own behalf? If the answer is no, please provide company name, address and telephone number of entity asserting claim.**

is asserting this CBI claim on its own behalf.

- 2. For what period do you assert your claim(s) of confidentiality? If the claim is to extend until a certain event or point in time, please indicate that event or time period. Explain why such information should remain confidential until such point.**

The information of the study report being claimed as CBI should be held confidential indefinitely.

- 3. Has the information that you are claiming as confidential been disclosed to any other governmental agency, or to this Agency at any other time? Identify the Agency to which the information was disclosed and provide the date and circumstances of the same. Was the disclosure accompanied by a claim of confidentiality? If yes, attach a copy of said document reflecting the confidentiality agreement.**

The report has not been disclosed to any other agency. It is possible that a robust summary of the study data, not including the information claimed as CBI, could be used in High Production Volume program submittals.

- 4. Briefly describe any physical or procedural restrictions within your company relating to the use and storage of the information you are claiming CBI.**

Access to the building where the Study Report is housed is restricted to _____ employees and to guests who are escorted by an _____ employee. An electronic version of the report is stored on a password-protected data server. Access to that server requires approval from the IT department as well as the Director of Environmental, Health and Safety.

- 5. If anyone outside your company has access to any of the information claimed CBI, are they restricted by confidentiality agreement(s). If so, explain the content of the agreement(s).**

The entities outside _____ who have access to the Study Report are restricted by confidentiality agreements with _____. These entities include the performing laboratory itself, a 3rd party consultant under contract to _____ to assist with the final data review and outside legal counsel which provides legal assistance and review of any submissions to a government agency.

's contract with the testing laboratory states:

All Studies, Study Protocols and other information developed for _____ by Laboratory in connection with the Work performed hereunder, the existence and conduct of any

FOR PUBLIC DISCLOSURE

discussion between the Parties, and the terms of this Agreement, shall also constitute Confidential Information . . . 's Confidential Information shall be held in strictest confidence by Laboratory and shall be used solely for purposes of performing the Work. Laboratory shall not disclose any of 's Confidential Information to anyone...

's Services Agreement with the 3rd party consultant states:

The consultant shall "hold 's Proprietary Information in strictest confidence, shall not disclose it to others, shall use it solely for purposes of performing such Service, and shall upon 's request, deliver to or destroy Proprietary Information . . . "

6. Does the information claimed as confidential appear or is it referred to in any of the following:

- a. Advertising or promotional material for the chemical substance or the resulting and product;
- b. Material safety data sheets or other similar materials (such as technical data sheets) for the substance or resulting end product (include copies of this information as it appears when accompanying the substance and/or product at the time of transfer or sale);
- c. Professional or trade publications; or
- d. Any other media or publications available to the public or to your competitors.

If you answered yes to any of the above, indicate where the information appears, include copies, and explain why it should nonetheless be treated as confidential.

While the *results* of the study will appear on Material Safety Data Sheets, the information claimed as confidential does not and will not appear in any of the materials listed above.

7. Has EPA, another federal agency, or court made any confidentiality determination regarding information associated with this substance? If so, provide copies of such determinations.

No.

8. Describe the substantial harmful effects that would result to your competitive position if the CBI information is made available to the public? In your answer, explain the causal relationship between disclosure and any resulting substantial harmful effects. Consider in your answer such constraints as capital and marketing cost, specialized technical expertise, or unusual processes and your competitors access to your customers. Address each piece of information claimed CBI separately.

A competitor, upon having easily obtainable access to the association between the company, the commercial product name identified in the study and the study details could use this information to their commercial advantage in an attempt to position an alternative to the product in the marketplace.

9. Has the substance been patented in the U.S. or elsewhere? Is a patent for the substance currently pending?

No patent application has been filed for this substance.

FOR PUBLIC DISCLOSURE

10. Is this substance/product commercially available and if so, for how long has it been available on the commercial market?

- a. If on the commercial market, are your competitors aware that the substance is commercially available in the U.S.?
- b. If not already commercially available, describe what stage of research and development (R&D) the substance is in, and estimate how soon a market will be established.
- c. What is the substance used for and what type of product(s) does it appear in.

is currently sold in the US and the EU as an intermediate for use in manufacture of curing agents for epoxy resins and chain extenders for polyurethanes. has been on the commercial market for approximately 20 years. Competitors would be aware that the substance is commercially available.

11. Describe whether a competitor could employ reverse engineering to identically recreate the substance?

Yes.

12. Do you assert that disclosure of this information you are claiming CBI would reveal:

- a. confidential processes used in manufacturing the substance;
No
- b. if a mixture, the actual portions of the substance in the mixture; or
No
- c. information unrelated to the effects of the substance on human health or the environment?

Yes

If your answer to any of the above questions is yes, explain how such information would be revealed.

It would reveal the company name, the commercial product name and the testing laboratory associated with the preliminary test report data being submitted for the chemical substance.

13. Provide the Chemical Abstract Service Registry Number for the product, if known. Is your company applying for a CAS number now or in the near future? If you have applied for a CAS number, include a copy of the contract with CAS.

The CAS Registry Number is 694-83-7.

14. Is the substance or any information claimed CBI the subject of FIFRA regulation or reporting? If so, explain.

No.